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A SYMPOSIUM ON DISTURBED ELECTROLYTE BALANCE IN CARDIOVASCULAR DISEASE

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Each month a major medical specialty is featured.

in this issue

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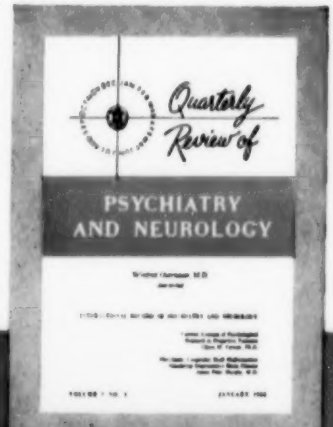
Winfred Overholser, M.D.
Editor-in-chief



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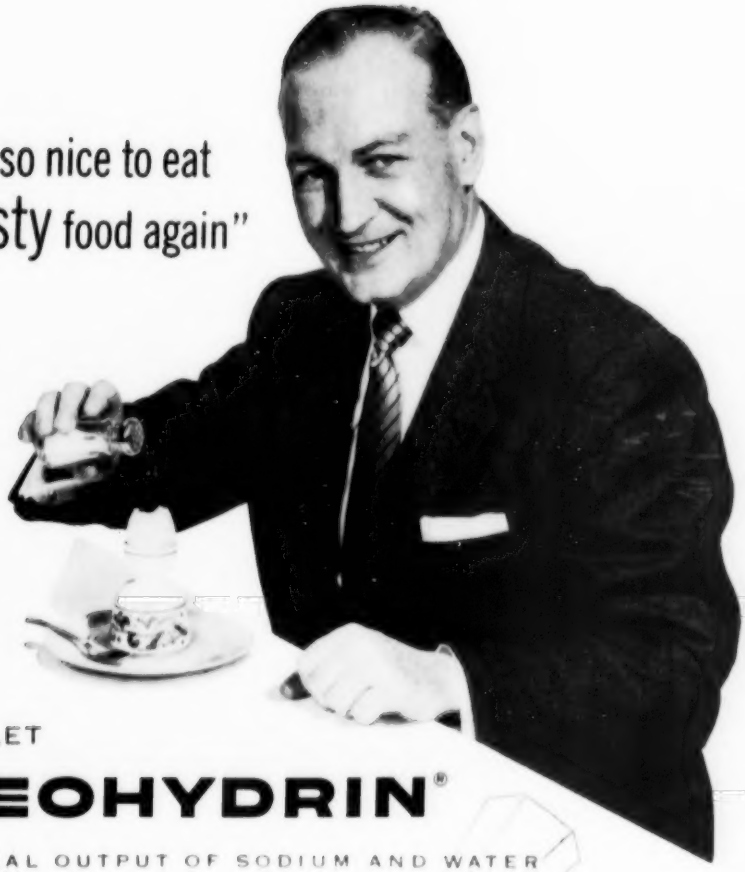

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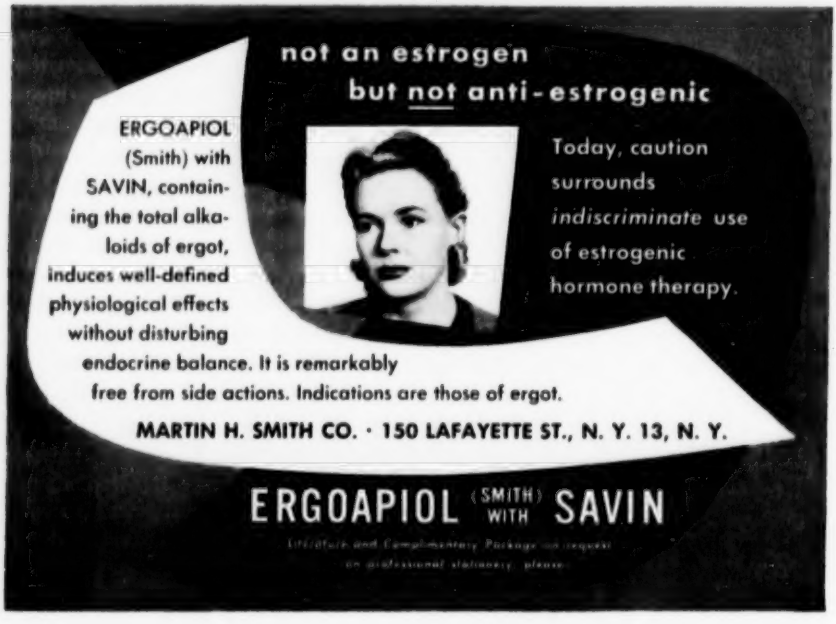
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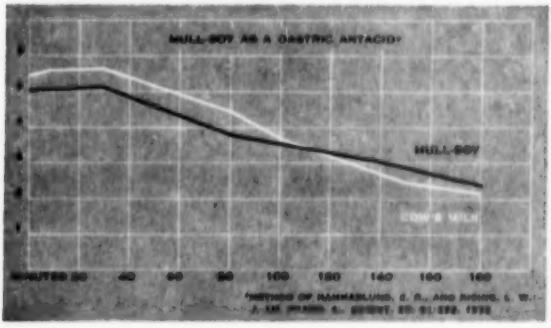

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A Symposium on Disturbed Electrolyte Balance in Cardiovascular Disease

INTRODUCTION

Electrolyte metabolism has come to be regarded as the key to therapy in congestive heart failure, hepatic cirrhosis, and other edematous syndromes. The current weight of evidence appears to support the likelihood that sodium retention in these clinical entities is mediated by adrenocortical action. Beyond this action, the underlying basis of the mechanism of edema is progressively less certain, but the importance of disturbed electrolyte metabolism as the *proximate* cause is unchallenged now. Regulation of intake is not notably successful for the restoration of normal electrolyte balance, but regulation of electrolyte *excretion* has produced gratifying results. Most successful among means of regulating electrolyte excretion is the use of organic mercurials.

Recollections of the frustrating clinical picture of edema in patients with congestive heart failure, before the advent of organic mercurial diuretic therapy, stand in distressing contrast to the optimistic outlook possible for patients of this generation. Both the prolongation of life and the usefulness of the added years realized through management with these diuretics would have seemed incredible a relatively short time ago. The mercurials have now become so much part and parcel of modern cardiac failure treatment that attention is no longer focussed on the lifesaving aspects of such management, but on the refinements in terms of balanced therapy and patient comfort.

The use of mercury compounds as diuretic agents dates back at least as far as Paracelsus, who used calomel to treat "dropsy." "Blue pills" or "Guy's Hospital pills," containing metallic mercury, were very widely used during most of the nineteenth century. The discovery of the diuretic efficacy of organic mercurial compounds did not stem from the previous use of inorganic mercurials but from an incidental clinical observation. In 1919, Alfred Vogl, then in his clinical clerkship in a Viennese hospital, noted the copious diuresis evoked by an antisyphilitic organic mercurial compound in a nonedematous young woman with congenital syphilis,

who was "probably, if anything, dehydrated." In a relatively brief time following publication of the initial observations with this compound, use of organic mercurial diuretics became widespread, and has since become almost universal. The physiologic basis of the mechanism involved, however, was not comprehended until the nineteen-thirties, when the interpretations of Cushny, Richards, and Homer Smith paved the way for the recognition that the increased urine flow could only be accounted for by inhibition of tubular reabsorption of sodium.

Within the framework of this electrolyte concept, the contributors to this symposium approach the clinical aspects of therapy with mercurial diuretics in terms of their own experience. The flexibility of treatment required to meet the broad range of reactions varies among patients, depending on the capacity for renal osmotic work. Suggested treatment regimes for the more important situations in cardiac failure are given by Schemm and Camara. Cole and Griffith stress the fact that great caution should be taken in the administration of bromides to patients with congestive heart failure, edema, and hypertension.

Advantages of oral administration from the standpoint of both convenience and therapeutic efficiency are discussed in the article by Bradford, who is joined by Donovan, Mauriello, and Leevy in reporting their initial clinical experience with the new oral mercurial diuretic, Neohydrin.* Both studies suggest the possibility of extensive use in ambulant cardiac patients.

Complications which may attend mercurial diuretic therapy, particularly when the low-sodium diet is used in conjunction with it, can be counteracted quickly upon recognition. In this connection, however, the physician must be able to distinguish readily between the salt-depletion syndrome and hypochloremic alkalosis. The clinical pictures and distinguishing characteristics of these two conditions, and their variant forms, are described by Holley and Hogan. The final contribution in this symposium presents the method devised by Gelfand for distinguishing between cardiac and bronchial asthma by observing the response to a single mercurial injection.

The papers presented here exemplify the progress that has been made in means of correcting the sodium retention underlying edema. Much of this success is the result of the use of mercurial diuretics. The opinions expressed in this symposium indicate how experimentation and clinical experience continue in the direction of expanded and more gainful use of these compounds.

Electrolyte Excretion in Congestive Heart Failure and the Role Played by Various Diuretics and Electrolyte Disturbances

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The idea that retention of sodium is a factor in the formation of edema was expressed as early as 1715 by Baynard[1] in the following words: "Salts creep with the chyle into the blood and have no way out but by the urine. . . ." Edema fluid, being merely an excess of extracellular fluid, contains electrolytes in virtually the same proportions as in normal extracellular fluid where sodium salts make up 90 per cent of the electrolyte present. This is true of the edema fluid of cardiacs, nephritics, and of the ascitic fluid of cirrhotics. It follows that for approximately each 9 Gm of sodium salts retained in edema, one liter of water is retained.

Basically there appears to be a separate control for these two factors: sodium being regulated by an adrenal cortical hormone, and water by the antidiuretic hormone of the posterior pituitary. In health, coordination between the two results in a relative constancy of the concentration of sodium and, with other factors concerned in homeostasis (such as acid-base balance), a relative fixity of volume of the extracellular fluid. While diminished excretion of sodium by the kidneys is considered to be the primary factor, this comes about according to this concept, not as a result of diminished renal function nor of diminished renal blood flow per se, but as part of a general response to some stimulus acting through the adrenal cortex. Evidence for this is the accompanying low excretion of sodium in sweat,[2,3] saliva,[3,4] and feces[5] in edema. Since a reduced concentration of sodium in the sweat, saliva, feces, and urine can be induced in normal subjects by the administration of ACTH and by desoxycorticosterone, it is assumed that increased production of adrenal cortical hormones is responsible for lessened excretion of sodium via these routes in all the conditions that produce edema.

A consideration of the osmotic work‡ performed by the renal tubules in the regu-

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‡The equation for osmotic work as formulated by von Rhorer[6] is as follows:

$$\text{Work} = NRT \times \left[\left(2.3 \log \frac{U}{B} \right) - \frac{U - B}{U} \right],$$

in which N = gram molecular weight of an excreted substance, R = the gas constant (1.987 cal. per degree); T = absolute body temperature 37° C. + 273° = 310° C.); U = concentration of the substance in the urine; B = concentration of the substance in the plasma, and 2.3 the factor to convert common logs to natural logs.

lation of the body content of sodium also challenges the concept that poor kidney function is the primary cause of sodium retention. For example, an individual who is in sodium balance on a daily intake of 150 mEq. will excrete in the urine about 145 mEq. of sodium daily, allowing 5 mEq. for skin and stool excretion. If the urine volumes were exactly 1 liter, no osmotic work has been performed, since the concentration of sodium in the urine is the same as its concentration in the plasma (145 mEq.). The same individual, still excreting one liter of urine a day, is now allowed to go into sodium balance on a daily sodium intake of only 8 milliequivalents. The liter of urine will contain about 2 mEq. of sodium, as compared with the still normal concentration of 145 mEq. per liter in the plasma. Here the conservation of sodium by the kidneys has been brought about by a considerable amount of osmotic work. If this necessary work cannot be performed, the result is a negative sodium balance, which occurs frequently in far advanced nephritics who have been placed on low sodium diets. The fact that strikingly low amounts of sodium are frequently found in the urines of edematous cardiacs is good evidence that their renal tubule cells are capable of reabsorbing sodium as well (i. e., doing as much osmotic work) as normal tubule cells. It is this capacity for tubular reabsorption of sodium which makes the edematous patient treated only by sodium restriction capable of a progressive increase in body sodium and edema.

Retention of water in the formation of edema is generally regarded as secondary to the mechanism of sodium retention described above. Increased production of antidiuretic hormone by the posterior pituitary has been shown to occur experimentally when hypertonic NaCl solution is injected into the internal carotid artery.[7] Clinical support of this experimental phenomenon has been obtained by demonstration of increased amounts of antidiuretic substance in the urine of cardiacs in congestive failure,[8] in nephrotics and edematous nephritics,[9] and in cirrhotics.[10]

These studies and concepts have helped clarify some of the aspects of the mechanism of edema formation, but as yet they have added no practical new tools for the prevention or elimination of edema to those now at our disposal. Nevertheless, they can be construed to explain in part why the restriction of sodium and administration of water, as outlined below, favors the excretion of sodium. Similar basic studies on acid-base factors may prove equally illuminating.

ELECTROLYTE EXCRETION AND A DIURETIC REGIME

Since sodium retention is so important in edema, its restriction is emphasized to such an extent that other adjuncts, which are useful in effecting its excretion, are often minimized or omitted. In *otherwise untreated* congestive heart failure, the urinary excretion of sodium may be reduced to a fraction of one milliequivalent (or less than 23 mg.) per day. Careful studies[11] have shown that even on as low a sodium intake as 8.6 mEq. daily (200 mg.) there is an obligatory insensible loss of sodium through the skin, amounting to approximately 5 mEq. a day, and a fecal loss of sodium, amounting to 2 mEq. or less. Thus, an *otherwise untreated* cardiac patient in congestive failure given an 8 mEq. sodium diet may have a total daily sodium excretion, through these various routes, of only 8 mEq. or *less* per day and

remain in balance with no loss of edema. Of course, if the patient's dietary intake of sodium were not restricted, there would be a very rapid accumulation of edema fluid. Even if the dietary sodium were restricted to a more practical level of 22 mEq. (506 mg.) a day, this otherwise untreated patient would still retain 14 mEq. (22 minus 8) of sodium daily and, thus, in only 10 days, would have retained 140 mEq. of sodium, the amount necessary to form one liter of extracellular fluid. Such studies indicate that in the management of resistant congestive heart failure more than simple sodium restriction is required for the excretion of the excess of sodium.

In the authors' experience, this can be most effectively carried out by a program in which the main features are a moderate salt restriction, an adequate fluid intake (adequate enough according to water-balance data to provide a liberal amount of urine-water), a neutral or acid-ash excess diet with daily administration of relatively small doses of acid diuretics, and the intermittent use of mercurial diuretics. Accepted measures such as rest (especially in a semirecumbent position), oxygen when necessary, and proper digitalization* are just as important, for they have long been known to produce, without even salt restriction, a diuresis of salt and water.

The rôle played by a high water intake in the diuretic regime, described in 1942 by the senior author, has been repeatedly emphasized.[12-16] Enough water is provided to enable the kidneys to carry away the retained sodium and other solid wastes and to maintain the extracellular fluid and the body cells in an optimal state of true hydration. As stated in 1942, a daily fluid intake of 2,000 ml. to 3,000 ml. is adequate for the *majority* of cases. However, in seriously ill cardiac patients with concomitant poor renal function, low-grade fever, hyperpnea, and excessive diaphoresis, the daily requirement for water for urine and temperature regulation is often as high, for example, as 4,000 milliliters. Furthermore, a preceding period during which the water intake has been deficient has often resulted in a large deficit of plain water, amounting not infrequently to 4,000 ml. (maximum about 7,000 ml.). [It has been experimentally shown[15] that no significant amount of sodium is excreted in the urine when normal subjects, as well as edematous cardiacs, are subjected to severe plain-water restriction. Even in subjects with normal kidneys when 2.5 to 3.5 liters of water are lost by evaporation (obligatory water loss for regulation of body temperature) over a period of two to three days, it is found that most of the sodium previously held in solution (140 to 145 mEq. per liter) by the water is retained. Such a plain-water deficit accounts for the notorious thirst of some edematous (or "brine-logged," *not* "water-logged") patients, and their plain water deficit must be corrected before a beneficent diuresis can occur.] Thus, in a patient with a previous plain-water deficit of 4,000 ml. and whose increased daily water needs amount to 4,000 ml., the estimated optimal water intake

*Digitalis produces sodium diuresis not by a direct action on the kidney, but indirectly through improvement of the heart action. This was thought to be due to relief of anoxia and improvement of the hemodynamics of the kidney. More recently, Earle and his co-workers[12] have produced suggestive, but not conclusive, evidence that digoxin does have a specific renal effect in blocking sodium reabsorption, aside from its effects on cardiac output or venous pressure.

would be 6,000 ml. daily for the first two days, and 4,000 ml. daily for some time thereafter.

The diet in this regime is designed to be either neutral or to contain a slight excess of acid ash over basic ash. This prevents the neutralization of the metabolic acids, which physiologically mobilize already stored sodium and prevent retention of the sodium taken in the diet. With such a diet and with mild acidification and adequate water intake, a diet containing 500 mg. to 1,000 mg. of sodium gives adequate restriction of this electrolyte.

This arrangement of the diet permits the use of smaller amounts of acidifying drugs. Ammonium chloride in doses of 1.5 Gm. to 4 Gm. daily (maximum 6 Gm.) is administered in a loosely packaged capsule (buffered with an equal amount of $CaCO_3$), rather than in the form of the relatively insoluble hard-packed, enteric-coated tablets, which roentgenologists and prosectors alike gleefully demonstrate as undissolved in large numbers in the lower part of the gastrointestinal tract. Balance studies carried out in the Metabolic Unit Laboratory show that ammonium chloride administered in the capsule is effectively absorbed and the chloride ion excreted in the urine.[27]

The aim in giving relatively small continuous daily doses of ammonium chloride instead of the customary large intermittent doses[18] is to keep up a constant mild threat to the hydrogen-ion concentration of the body fluid, rather than to produce an intermittent intense acidosis which quickly invokes ammonia production and its excretion in place of sodium;* thus, there is a steadier loss of retained sodium and, in addition, no troublesome gastrointestinal upsets. The authors' experimental data[27] indicate that in the long run the continuous daily administration of smaller amounts of this acidifying drug proves more beneficial than the method of giving large intermittent doses of it.

The striking diuretic action of mercurials is apparently not associated, in man,[19] with either increase in glomerular filtration or renal plasma flow. Their action is believed to be on the distal tubule and to interfere through some enzyme-inhibiting action with the distal tubular reabsorption of sodium. In the ordinary case of congestive heart failure, mercurials are given only with the idea of accelerating the sodium diuresis produced by the regime described above. They are useful (1) in shortening the necessary period of hospitalization of most patients who would ordinarily, though slowly, respond to the regime; (2) to hasten relief in seriously ill patients with massive anasarca and marked discomfort therefrom; and (3) their use is imperative in some resistant cases which will not respond to all the other measures. It should be emphasized that the mercurial diuretic is not the final answer to the occasional truly resistant case whose edema will not yield to the most rigidly imposed measures, and in whom the only reward for repeated mercurial

*More recently, it has been shown[17] that when ammonium chloride is given by Gamble's method,[18] with each subsequent period of ammonium chloride administration the amount of sodium excreted with the chloride diminishes rapidly as the body stores of sodium are depleted, and more base in the form of potassium is eliminated.

administration is the development of hyponatremia, hypokalemia, or some other chemical abnormality which may in itself have an antidiuretic effect.

In the authors' Metabolic Unit, they have had the opportunity of carrying out electrolyte balance studies in scores of cases with severe and resistant congestive heart failure while undergoing treatment. This has enabled the authors to observe the effect on diuretic response to the regime and to the correction of electrolyte pattern disturbances. The Unit has its own laboratory with two chemists, its own diet kitchen with a certified dietitian, and an experienced nursing supervisor. The Illustrative Cases give a few examples of the data obtained, and the usefulness of the data in therapy.

Balance, of course, means the difference between total intake (dietary plus supplementary sodium or potassium intake given orally or intravenously) and the total output, which includes urinary, fecal, and estimated skin loss, as well as that lost by emesis or by any drainage (thoracentesis, paracentesis, gastric or intestinal suction, etc.). In these calculations, the skin and fecal losses are estimated and the figures used are based on those obtained by Arn and Reimer.[11] The daily dietary intake of sodium, potassium, protein, the caloric intake and excess of acid ash or basic ash in the food is calculated from the figures given by Bowes and Church[26] for the food actually ingested.

Method: Upon admission the patient's height and weight are recorded, and from then on daily fasting weight in the morning is recorded on a scale which is sensitive to 100 grams. Twenty-four hourly urine specimens are collected daily, collections being started and ended at 6:00 a.m. daily and their volumes recorded. The daily urinary excretion of chloride,* sodium and potassium† are determined. The morning following admission, blood specimens are obtained in the fasting state for initial blood chemistry. The chemistry includes plasma sodium, potassium, chloride,‡ CO_2 combining power, serum proteins, urea N, cholesterol, blood *p*H, and plasma specific gravity, and osmotic pressure.§ The same set of chemistry is obtained at appropriate intervals and at the end of treatment. In suitable cases D_2O, thiocyanate and Evans blue spaces are determined before and after loss of edema.

ILLUSTRATIVE CASES

Group I. Patients who Respond to the Regime Without the Use of Mercurial Diuretics

a) F.C., male, age 70: Admitted with diagnosis of hypertensive and arteriosclerotic heart disease. He had congestive failure manifested by pulmonary and hepatic passive congestion, severe orthopnea, and marked dependent edema. His blood pressure was 240/180.

*Urine chlorides are determined by the method of Sendroy as modified by Van Slyke and Hiller.[29]

†Sodium and potassium determinations are carried out with a Beckman flame photometer.

‡Plasma chlorides are determined by the method of Osterberg and Schmidt.[23]

§Osmotic pressure values on plasma samples are obtained by the thermoelectric method of Baldes and Johnson.[24,25]

‖D_2O concentrations in plasma and urine are determined by the falling drop method of Cohn,[27] and thiocyanate determinations are carried out by the method of Barker.[28]

Patient F. C.: Data Showing Sodium and Potassium Balances During a Five-day Period

Electrolyte	Output				Intake	Balance
	Urine	Skin (est.)	Stool (est.)	Total	Dietary mEq.	mEq.
	mEq.	mEq.	mEq.	mEq.		
Sodium	1,372	235	7	1,614	46	−1568
Potassium	298	50	15	363	273	−90

During this five-day period in the early part of hospitalization, F. C. took by mouth an average of 3,700 ml. of water daily; the diuretic medications consisted of 4 Gm. of ammonium chloride daily and a rapid digitalization. His "neutral" diet yielded an average sodium content of 9.2 mEq. daily. During this period there was a total negative sodium balance of 1,568 milliequivalents. The average plasma Na concentration was 143 mEq. per liter. If 1,568 is divided by 143, the result is 10.9 liters, the amount of extracellular fluid the patient should have lost with that amount of body sodium excreted. Actually, with complete clearing of edema there was a weight loss of 13.5 Kg. (weight dropped from 119.7 Kg. to 106.2 Kg. in this five-day period). The discrepancy here could be explained by the fact that the authors had estimated too little sodium loss through the skin.

Calculations for potassium during the same period showed a negative balance of 90 mEq., most of which can be accounted for by the loss of 13.5 liters of extracellular fluid, the average K concentration of which was 4.3 mEq. per liter (13.5 x 4.3 = 58.1 mEq.).

(b) L. H., female, age 79: Arteriosclerotic heart disease; she was anasarcous on admission, and had bilateral hydrothorax, hepatic passive congestion and grotesque edema from the toes up to the level of the tenth dorsal spine in the back. The blood pressure was 140/80. She had never been under a physician's care before.

Patient L. H.: Sodium and Potassium Balances During a Thirteen-day Period

Electrolyte	Output						Intake	Balance
	Urine	Chest fluid	Emesis	Skin (est.)	Stool (est.)	Total	Dietary mEq.	mEq.
	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.		
Sodium	2,250	88	6	65	20	2,429	166	−2263
Potassium	579	3	6	65	12	665	458	−207

Upon admission the regime was instituted with prompt digitalization and administration of 4 Gm. of ammonium chloride daily. The average oral fluid intake during the 13 day period under consideration was 2,350 ml. daily. The total negative sodium balance being 2,263 mEq. and the average plasma sodium concentra-

tion 145 mEq. per liter, the estimated amount of extracellular fluid loss (2,263 divided by 145) was 15.6 liters. During this period, the plasma sodium rose from 140 to 150 mEq. per liter. Since the extracellular fluid volume in this patient as determined by the thiocyanate space method was 18 liters, 180 mEq. of sodium (18 times 10) can be accounted for by the rise in plasma sodium concentration. This is equivalent to 1.24 liters of extracellular fluid had this amount of sodium been lost from the body. Therefore, the expected extracellular fluid loss would have been 16.8 liters (15.6 plus 1.2). This compares with an actual weight loss of 18.4 Kg. in this 13 day period, the weight having dropped from 72.4 to 54.0 Kg. with the clearing of all signs of edema.

In this patient the thiocyanate and D_2O spaces before and after clearing of edema were determined. The change in thiocyanate space was 15.4 liters, and in the D_2O space it was 14.3 liters. Since this patient was eating a close-to-maintenance diet during this period when she was almost totally inactive (average 1,250 cal. per day), it may be said that estimation of extracellular fluid loss by sodium balance studies gives a closer approximation to actual weight loss than either the thiocyanate or D_2O space determinations.

During the same period, L. H. had a negative potassium balance of 207 mEq., of which 92 mEq. can be accounted for by the loss of extracellular fluid. That the actual negative potassium balance of 115 mEq. (4.2 Gm. of K) was not sufficient to cause a significant depletion of body potassium is shown by the fact that the plasma K during this period actually rose from 4.7 to 5.2 mEq. per liter.

As previously mentioned, the plasma sodium concentration rose from 140 to 150 mEq. per liter during this period of observation. There was a concomitant increase in plasma osmotic pressure from 154 to 170 mOsmols per liter, and in plasma specific gravity from 1.0257 to 1.0286. The authors interpret this to mean a disproportionately greater loss of water than of sodium from the extracellular fluid compartment, and this could account for the discrepancy between weight loss (16.8 Kg.) as predicted from the negative sodium balance and the actual weight loss (18.4 Kg.).

Group II. Patients Treated With the Regime and With the Aid of Mercurial Diuretics. These are the moderately resistant cases whose edema does not respond rapidly enough to the regime alone to make withholding of mercurial diuretics advisable when discomfort from the fluid accumulations is extreme, or practical from the economic point of view.

(a) W. H., housewife, age 43: Marked congestive failure due to hypertensive and arteriosclerotic heart disease with bilateral hydrothorax, ascites, hepatic passive congestion, and deep peripheral edema extending from the feet up to the upper interscapular areas and involving even the arms. She had had diabetes for at least nine years, hypertension during the past two years, and known albuminuria for at least a year. Exertional dyspnoea started six years prior to admission, and she went into frank congestive failure four years later. During the two years prior to admission, she had spent long periods of hospitalization in Canada for relief of congestive failure. Prior to her transfer here she had been confined for four months in a

hospital in Canada where she had been treated by digitalization, restriction of dietary sodium, administration of ammonium chloride, and injections of mercurial diuretics every second day; there was no relief of the edema. Two weeks before admission to the Unit, paracentesis was done with very little drainage. A week later Southey tubes were inserted into both legs with the hope of draining the edema fluid mechanically, also to no avail. The blood pressure was 200/140.

Patient W. H. Data on Sodium Balance During a Twenty-eight day Period

Output				Intake	Balance
Urine	Skin (est.)	Stool (est.)	Total	Dietary	mEq
mEq	mEq	mEq	mEq	mEq	
2,144	150	90	2,324	242	−2,082

This patient was in the Unit 28 days during which time treatment consisted of the usual rest, mild sedation, redigitalization, a neutral diet with sodium restriction, 2 to 4 Gm. of ammonium chloride per day, an adequate fluid intake averaging 3,000 ml. daily (attained with supplementary intravenous infusions of 500 to 1,000 ml. of 5 per cent dextrose in distilled water daily during the first 11 days), and eight intermittent doses of thiomerin given at three to four day intervals. By the fourth day on this regime, *before* the first dose of thiomerin was given, W. H. had lost 4.7 Kg. with a urinary sodium diuresis of 537 milliequivalents. The total urinary sodium excretion was 2,144 mEq. (equivalent to 125.4 Gm. of NaCl), and the total negative sodium balance 2,082 milliequivalents. This figure divided by 147 (the average plasma sodium concentration per liter) gives 14.2 liters, the amount of extracellular fluid which should have been lost. The actual weight loss was very close to this figure, being 14.5 Kg. (from 76.5 to 62.0 Kg.).

(b) H. M., female, age 38: Rheumatic heart disease with a severe grade of mitral stenosis and moderate mitral insufficiency. Signs of congestive failure had started two years prior to admission and during the past year she had spent five and one-half months in different hospitals without obtaining relief from orthopnea, epigastric distress, and edema, in spite of thoracentesis and many doses of mercurial diuretics. There was auricular fibrillation with a rate of 140 per minute on admission. She had signs of severe pulmonary congestion, hydrothorax on the right side, hepatic passive congestion, ascites, deep brawny edema of the lower extremities, and general fullness of the body including the upper extremities. The skin, particularly on the lower extremities, presented a livid cyanosis. An indolent ulcer was present over the left malleolus.

On admission she was placed in an oxygen tent, rapidly digitalized with the initial doses of digitalis given intravenously, administered frequent doses of adrenalin for orthopnea, and was sedated with morphine, followed later by phenobarbital. As soon as it could be tolerated, ammonium chloride was administered in daily doses of 1.5 Gm. during the first four days, subsequently increased to 3 Gm.

daily. She received four doses of thiomerin at intervals of four to five days. The daily fluid intake averaged 3,800 ml.; this included an occasional supplementary intravenous infusion of 500 ml. of 5 per cent dextrose in distilled water.

The 176 mEq. of sodium administered intravenously, as shown in the above table, were given to correct signs and symptoms of hypovolemia (nausea, hematocrit of

Patient H. M. Sodium and Potassium Balance During a Twenty-day Period

Electrolyte	Output					Intake			Balance
	Urine	Chest Fluid	Skin (est.)	Stool (est.)	Total	Dietary	I. V. Infusions	Total	
	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.
Sodium	2,014	34	100	35	2,183	191	176	367	−1,816
Potassium	603	1	95	57	756	697		697	−59

64 per cent, rbc of 6.7 M. per cu. mm. and Hb of 20.8 Gm. per cent, with previous values of 48 per cent, 4.8 M. per cu. mm. and 14.2 Gm. per cent respectively) which developed following the last dose of thiomerin. The average plasma sodium concentration being 142 mEq. per liter, the negative sodium balance of 1,816 mEq represented a loss of extracellular fluid amounting to 12.8 liters. Actually, the weight loss was 13.7 Kg. (from 59.7 to 46.0 Kg.). Caloric intake during this period was adequate, averaging 1,800 calories daily. In this patient, the thiocyanate space diminished by 11.8 liters, and the D_2O space by 14.8 liters during the same period of observation.

This patient remained in potassium balance throughout the course of treatment without supplementary potassium medication. The apparent negative balance of 58 mEq. can all be accounted for by the loss of about 14 liters of extracellular fluid with the clearing of the edema (14 times 4.3, the average plasma K concentration, gives 60 mEq. of potassium lost with clearing of edema), and the plasma potassium remained within normal limits: from 4.6 to 4.0 mEq. per liter.

Group III. Patients Who Develop Potassium Deficiency with the Use of Mercurial Diuretics. This curious phenomenon has been observed in some of the authors' patients in whom it has been possible to avoid a disastrous degree of potassium deficiency only by constant watching of their potassium plasma levels and of their urinary potassium excretion, and by judicious administration of potassium salts.

Most of the patients in congestive heart failure get rid of their edema on the diuretic regime without developing potassium deficiency. As in normal subjects, their kidney tubules are able to reabsorb selectively the necessary amount of potassium from the glomerular filtrate to maintain potassium balance, even in the face of a diuresis of sodium caused by the mercurial administered. Evidently, in the patients to be described here, the kidney tubules have lost the power of selectively reabsorbing potassium, and a dose of mercurial diuretic causes as much, if not more, urinary output of potassium than of sodium. Two cases will be presented, the first

one of whom manifested this phenomenon to a marked degree.

(a) R. M., female, age 56: Severe rheumatic heart disease with a marked degree of mitral and aortic valve involvement. She had rheumatic fever at 18 years of age. Onset of auricular fibrillation came at 32 years of age.

The patient had been in congestive failure for two years before she was first seen in 1949. From then on there followed a long series of admissions with a progressively intractable edema. During the last two hospitalizations in 1952, each lasting almost four months, the edema cleared very slowly even with the most heroic measures and it was then that potassium balance could be maintained only by constantly supplementing dietary potassium with oral, and sometimes intravenous, doses of potassium chloride. During an earlier admission (1950), it had been shown that the edema would clear up only with adequate daily potassium supplements (6 Gm. of KCl daily). Electrolyte balance studies were carried out throughout her stay. There have been selected certain periods during her sojourn which demonstrate the development of hypokalemia following a period of negative potassium balance and correction of hypokalemia by vigorous replacement with potassium salts, following which otherwise intractable edema responded.

Patient R. M.: Two Periods Showing Effect of Potassium Deficiency and Its Replacement on Plasma Potassium Levels

Period	Output				Intake			Balance	Change in Plasma K
	Urine	Skin (est.)	Stool (est.)	Total	Dietary	Suppl. KCl	Total		
	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq./L.
I (4 days)	393	15	20	428	103	95	198	−230	5.2 to 2.8
II (2 days)	18	10	6	34	46	161	207	+173	2.8 to 4.7

From March 6 to March 10, 1952, this patient had nausea and repeated emesis, was able to retain only small amounts of food and could not tolerate much oral medication. On the third day of this period, when 3 ml. of thiomerin were administered by vein, the urinary potassium output was 216 mEq. as compared to the urinary sodium diuresis of only 118 mEq. on the same day. There was a total negative potassium balance of 230 mEq., and this was reflected in the development of hypokalemia (2.8 mEq. per liter).

There was a negative sodium balance of 179 mEq. for the corresponding period, and the plasma sodium concentration being 126 mEq. per liter, this was equivalent to the loss of 1.4 liters of extracellular fluid. The actual weight loss was 1.9 kilograms.

During the succeeding two days, the patient was able to retain food and to take KCl (buffered with equal amounts of $CaCO_3$ in a capsule) by mouth. The hypoka-

lemia was promptly corrected, so that by the morning of March 12, the plasma potassium had risen to 4.7 mEq. per liter, during this two day period. There was a positive potassium balance of 173 milliequivalents.

For several other periods during her prolonged hospitalization fluctuations in the level of plasma potassium could be accounted for by either negative or positive potassium balance.

(b) R. T., female, age 37: Advanced rheumatic valvular heart disease involving both mitral and aortic valves, had been repeatedly admitted to the Unit for relief of congestive heart failure. Rheumatic fever "licked her joints and bit the heart" when she was 12, and her heart has been fibrillating since she was 22 years of age. In the last four years, she has had several embolic phenomena, the last one resulting in permanent dysarthria. During her last few admissions, she has manifested the same tendency to develop hypokalemia with institution of the diuretic regime, but not to as marked a degree as in the patient described above.

Patient R. T.: Data on Potassium Balance Studies

Period	Output				Intake			Balance	Change in Plasma K
	Urine	Skin (est.)	Stool (est.)	Total	Dietary	Suppl. KCl	Total		
	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq./L.
I (6 days)	361	35	21	417	244	—	244	−173	4.1 to 3.5
II (12 days)	689	60	36	785	452	643	1095	+310	3.5 to 4.3

Negative potassium balance amounting to 173 mEq. occurred during the first period, when she received two doses of thiomerin and no supplementary potassium medication. Of this amount 10 mEq. (2.5 liters times 4.1 mEq.) could be accounted for by loss of extracellular fluid with edema loss, so that the actual potassium deficit was 163 milliequivalents. It is interesting to note that following the second dose of thiomerin the urinary output of potassium was much greater than that of sodium: 189 mEq. of potassium as against 39 mEq. of sodium.

During the next 12 days, the patient received supplementary potassium chloride by mouth amounting to 48 Gm. or 643 mEq. of potassium. She had a positive potassium balance of 310 mEq., and this was reflected in the plasma potassium concentration which rose from 3.5 to 4.3 mEq. per liter. The edema yielded more promptly to the diuretic measures after attention was paid to maintenance of potassium balance.

Group IV. Patients Whose Edemata Remain Intractable Until Hyponatremia is Corrected by Administration of Hypertonic NaCl Solution. In this group are those cases which have badly degenerated hearts and are usually terminal.

(a) B. S., female, age 65. Rheumatic valvular heart disease with mitral stenosis and concomitant hypertensive and arteriosclerotic heart disease. The patient went into frank congestive failure two years before admission. When she came to the Unit, she was orthopneic and had frequent severe episodes of paroxysmal dyspnea. The heart was markedly enlarged and was fibrillating. She had bilateral hydrothorax, hepatic passive congestion, ascites, and marked dependent edema.

Patient B. S.—Balance Studies Showing Development of Hyponatremia and Its Correction by the Use of Hypertonic NaCl Solution

Period	Output						Intake			Balance	Change in Plasma Na	Weight Change
	Urine	Chest Fluid	Abd. Fluid	Skin (est.)	Stool (est.)	Total	Dietary	I. V.	Total	mEq.	mEq./L.	Kg.
	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.			
I (10 days)	262	156		50	12	480	41	133	174	−306	143 to 118	+2.6
II (11 days)	1551	90	39	55	15	1750	164	1246	1410	−341	118 to 145	−9.0

The plasma sodium on admission was 143 mEq. per liter. She received 1 ml. of thiomerin on the third, and again on the sixth hospital day, with practically no weight loss. On the twelfth day, she weighed 2.6 Kg. (53.8 Kg.) more than she did on the day of admission (51.2 Kg.), despite the facts that she had had the two doses of thiomerin and a total of 1,350 ml. of chest fluid had been aspirated from both pleural cavities. On that day the patient was in a coma. The plasma sodium was found to have dropped to 118 mEq. per liter. The plasma potassium was 4.4 mEq. per liter. The sodium balance at that point may be seen from the table above. As previously pointed out, there was a weight gain of 2.6 Kg. Assuming the average plasma concentration of sodium during that period to be 130 mEq. per liter, the amount of water retained (2.6 liters) took up about 338 mEq. more of sodium for solution (2.6 x 130 = 338). Therefore, the actual "loss" of sodium to the body was 644 mEq. (306 plus 338 mEq.). The edema-free weight of this patient being only 36.5 Kg., the normal extracellular fluid volume for her was probably 7 liters. The excess weight at that time was 16 Kg., so that the extracellular fluid volume may safely be assumed as 23 liters. By dividing 644 mEq. by 23 liters, we obtain the figure 28 mEq. per liter which is the expected drop in the plasma sodium concentration. The actual drop was 25 mEq. per liter (from 143 to 118 mEq. per liter).

Hyponatremia in this patient was promptly corrected by the administration of hypertonic NaCl solution (800 ml. of 3 per cent NaCl) plus 200 ml. of molar solution of sodium lactate. This was followed by four intermittent 500 ml. infusions of 0.45 and 0.9 per cent NaCl in the succeeding seven days to prevent a recurrence of hyponatremia. The plasma sodium concentration on the day following adminis-

tration of the hypertonic salt solutions was 148 mEq. per liter, and B. S. promptly roused from her coma. During the 11 days following correction of hyponatremia, the edema responded well to thiomerin injections, and the patient lost a total of 9.0 Kg. of edema weight. She was then almost free of edema. She died suddenly and unexpectedly a month later when she apparently was doing well.

b) G. G., female, age 42: Severe rheumatic heart disease. The patient demonstrates the not infrequent failure of hypertonic NaCl solutions to correct hyponatremia.

The patient had been in congestive failure with repeated hospitalization for some six years prior to this admission to the Unit. She showed a grossly enlarged fibrillating heart, extreme hepatic and pulmonary passive congestion with hydrothorax on the right side, ascites, and marked dependent edema. The plasma sodium concentration on admission was 113 mEq. per liter. Attempts were made to correct this by administration on different days of 3, 5, and 6 per cent NaCl in amounts varying from 400 to 500 milliliters. During a 10 day period the sodium given intravenously in this form amounted to 1,345 mEq., whereas the dietary sodium intake for the whole period was only 9 milliequivalents. The urinary, skin, and fecal loss of sodium was 366 milliequivalents. There was then a positive sodium balance of 988 milliequivalents. These heroic efforts resulted only in a transient rise of plasma sodium to 125 mEq. per liter and were rewarded by further increase in edema with a total weight gain of 4.7 Kg. (from 57.8 to 62.5 Kg.). Terminally, the plasma sodium concentration was 110 mEq. per liter. She died following several convulsive episodes.

Group V. Patients Who Manifest the So-called "Sump" Phenomenon. These cases constitute a most interesting group in the authors' series. In these patients one of the serous cavities, usually one of the pleural cavities and sometimes the abdominal cavity acts like a "low pressure" area in which edema fluid accumulates in transit to or from the peripheral tissues. During the process of clearing of edema, fluid keeps recurring in such a cavity after each tapping, and in the end most of the edema weight loss can be attributed to the amount of fluid removed mechanically. Between aspirations, signs of fluid in the low pressure area just tapped *increase*, while signs of peripheral edema *decrease*, without appreciable weight change. Sodium loss through the kidneys is relatively small despite the use of mercurials. Among such patients, recurrence of peripheral edema is preceded by reaccumulation of fluid in the "sump," and the appearance of edema can be forestalled by repeated tapping.

a) F. J., male, age 52: A high-grade pure mitral stenosis resulting from recurrent episodes of rheumatic fever in childhood. He demonstrated the "sump" phenomenon to a remarkable degree. Manifestations of congestive failure had appeared before he was seen by the authors, and during the preceding six months he had been repeatedly hospitalized, with no relief following institution of the customary low sodium diet with acid diuretics and frequent doses of mercurial diuretics. Digitalis was being given; massive right hydrothorax had had to be aspirated on several occasions. On admission, he was deeply cyanotic, mentally confused, anasarcous,

he had peripheral edema reaching half way up the torso, bilateral hydrothorax, ascites, and marked hepatic passive congestion (lower border of the liver 5 inches below the right costal margin).

He was promptly redigitalized, placed in an oxygen tent and the high fluid, neutral diet and ammonium chloride regime instituted. He received supplementary water (5 per cent dextrose in distilled water) by intravenous infusions daily during the first five days (amounting to as much as 2,700 ml. by vein in one day). These supplements brought his total fluid intake to an average of 3,200 ml. daily during that period. Following proper hydration, repeated intermittent doses of thiomerin, both by muscle and by vein, resulted in relatively little sodium diuresis. Most of the actual edema weight loss could be attributed to the amount of fluid mechanically removed from the right pleural cavity. Thoracentesis was performed eight times at intervals of two to nine days on the right pleural cavity only. The amount of fluid removed ranged from 2,800 ml. with the second thoracentesis to 750 ml. removed during the last procedure while he was in the hospital. The total amount of fluid removed mechanically was 14.02 liters, and the actual edema weight loss during that period was 16.1 Kg. (70.3 Kg. to 54.2 Kg.). At the time of discharge, he was edema-free, but subsequently the right pleural cavity had to be tapped repeatedly to prevent recurrence of peripheral edema and hepatic passive congestion.

Patient F. J.: Data on Sodium Balance Studies on a Patient Most of Whose Edema Weight Loss Can Be Attributed to Repeated Aspiration of Chest Fluid During a 29-Day Period

Output						Intake	Amount Chest Fluid Aspirated	Edema Weight Loss	Weight Loss Due to Fluid Aspirated
Urine	Chest Fluid	Emeses	Skin (est.)	Stool (est.)	Total	Dietary	Liters	Kg.	Per cent
mEq.	mEq.	mEq.	mEq.	mEq.	mEq.	mEq.			
435	1,794	32	145	43	2,449	255	14.02	16.1	88

The sodium balance studies show the relatively small percentage of retained body sodium removed through the kidneys to achieve a "dry weight." There was a total negative sodium balance of 2,174 mEq. This figure, divided by 137 mEq. (the average plasma sodium concentration), gives 15.9 liters of extracellular fluid which should have been theoretically lost. This tallies very closely with the actual edema weight loss of 16.1 kilograms. Here 88 per cent of the excess sodium lost by-passed reluctant kidneys to achieve a "dry weight."

(b) B. O., housewife, age 60: This patient with hypertensive arteriosclerotic heart disease in congestive failure demonstrated the "sump" phenomenon to a lesser degree. She had developed dependent edema and dyspnea seven months prior to her coming to the Unit, and during the three months preceding admission, the right pleural cavity had been tapped every five to six days, while she was receiving mercurial diuretics also every five to six days.

On admission, she had a grossly enlarged heart that was fibrillating, a right-sided hydrothorax, some ascites, a grossly distended liver whose lower margin extended 5 inches below the right costal margin, and a moderate amount of peripheral edema.

Patient B. O.: Data on Sodium Balance Studies in a Patent Who Underwent Repeated Thoracentesis During a 10-Day Period

Output						Intake	Amount Chest Fluid Aspirated	Edema Weight Loss	Weight Loss Due to Fluid Aspirated
Urine	Chest Fluid	Emeses	Skin (est.)	Stool (est.)	Total	mEq.	Liters	Kg.	Per cent
mEq.	mEq.	mEq.	mEq.	mEq.	mEq.				
743	388	8	50	15	1204	60	2.85	7.5	38

In this 10 day period during which the right pleural cavity was drained four times of a total amount of 2.85 liters, the corresponding edema weight loss was 7.5 kilograms. B. O. received five doses of mercuhydrin during that period. There was a total negative sodium balance of 1,143 mEq., and having an average plasma sodium concentration of 142 mEq. per liter, that amount of sodium represented a loss of 8 liters of extracellular fluid. The actual edema weight loss of 7.5 Kg. comes close to that figure.

It will be noted that in this patient the removal of "sump" fluid accounted for only 38 per cent of edema weight loss, in contrast to 88 per cent in the case of patient F. J., but utilization of the sump phenomenon enabled us to attain a dry weight in 10 days, which had not been attained in the preceding seven months.

SUMMARY AND CONCLUSIONS

Sodium retention is the primary factor in the formation of edema. Water is retained in proportionate amounts, such that the electrolyte concentration of edema fluid corresponds to that of normal extracellular fluid. An adrenal cortical hormone and the antidiuretic principle from the posterior pituitary regulate the sodium and water content of the body through their influence on the kidney, and it appears that in edema, such as in congestive heart failure, nephritis, and cirrhosis of the liver, there is excessive production of both hormones.

The aim of any diuretic regime is the mobilization of the retained sodium and its excretion through the kidneys. The effectiveness of a program which includes an adequate water intake, a neutral or acid-ash diet with moderate salt restriction, mild acidification, and the use of mercurial diuretics is discussed. The importance of indirect adjuvant diuretic measures such as rest, use of oxygen, and full digitalization is pointed out.

The results of careful electrolyte balance studies in edematous cardiac patients undergoing treatment are described in detail. It is shown that the edema weight loss can often be quite accurately predicted from the amount of negative sodium balance. Where minor discrepancies exist they can usually be accounted for by evidence of concentration of body fluid, or shift of water to dehydrated cells, or incorrect estimates of fecal and skin losses of sodium.

Attention is called to the resistant cases who develop serious electrolyte disturbances, such as hyponatremia and hypokalemia as a result, for example, of vigorous use of mercurial diuretics. In such cases, diureses can be effected and disaster averted only by proper electrolyte replacement.

Mention is made of the utilization of a "sump" phenomenon to achieve a dry weight in part or in whole, when the kidneys resist efforts to effect sodium excretion by means of the methods discussed above.

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Bromism and Salt Balance in Cardiovascular Disease

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Bromism should be suspected when central nervous symptoms appear in individuals whose salt intake has been restricted and output increased. The salt output of patients with cardiovascular disease long has been accelerated by the use of mercurial diuretics.[1] In addition, exchange resins[2] recently have become available which produce fecal removal of sodium ions. Under these circumstances, bromides may have an effect out of all proportion to the size of the dose administered.

Low-sodium regimens[3] have widespread use in the treatment of congestive heart failure and have been recommended for the management of hypertension.[4] When the sodium ingest is suppressed to 200 mg.[5] or less,[6] even the tap water[7] of some localities has been identified as a relatively substantial source of that ion.

It should be emphasized that since most of the sodium in the diet is in the form of salt,[8] attempts to decrease sodium will lower the chloride intake and thus favor the development of bromide intoxication. When the sodium is kept below 200 mg., the chloride of the daily diet is reduced from the average normal of 10 Gm. to 300 milligrams. As this marked restriction produces a decrease in body chloride, bromide,[9] when present, will substitute proportionately for the deficient halogen and accumulate in the tissues. Under these circumstances, the administration of bromides in seemingly safe amounts may rapidly lead to bromide intoxication. The retention of bromides[10] may be further augmented by retarded halogen excretion in individuals with impaired renal function. This may be of importance to individuals with cardiac congestive failure who have diminished renal plasma flow, decreased glomerular filtration rate, and lowered sodium excretion.

In addition, patients may be taking self-administered bromides without the knowledge of the physician who has restricted their sodium chloride intake. The patients themselves often do not know that the proprietary products they obtain without prescription contain bromides.

To determine the significance of these factors, all the known cases of bromism in the Cedars of Lebanon Hospital from 1931 to 1951 were reviewed. Nine of the twelve cases found were admitted after 1942, when low-sodium regimens again

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became popular in the management of heart failure and hypertension.* Three patients manifested cardiovascular disease for which their sodium intake was restricted. Their case histories are briefly summarized in the following paragraphs.

CASE MATERIAL

Case 1. A woman 62 years old entered the hospital on July 5, 1949, with an initial diagnosis of hypertensive encephalopathy to explain mental retardation and confusion. About two and one-half months previously, the patient had been placed on a salt-free diet because of hypertension and left heart failure. During the month prior to admission, 16 oz. of elixir triple bromides were known to be consumed. On July 1, she fell on the way to the bathroom; she did not remember whether she tripped on a rug or her right leg just buckled up under her. It was noted that there had been increasing mental confusion, slurring of speech, slowing of reaction time, and, more recently, fears and hallucinations during the night. Physical examination revealed an elderly white woman who joked a lot and became excited easily. She misnamed things, misinterpreted questions, and had difficulty remembering events. Her speech was slurred and there was marked perseveration. Her blood pressure was 180/110. Fundoscopic examination showed clear disc margins. Her deep reflexes were depressed throughout; the abdominal reflexes were absent. There was a positive Oppenheim on the right side. Examination of the spinal fluid showed a pressure of 120 mm. of water. It was clear, colorless fluid, with one cell, total protein 52, chlorides 680, sugar 69. The Gold curve was normal and Wasserman tests were negative. Urinalysis, complete blood count, blood sugar, cholesterol, NPN, serum chlorides, and CO_2 combining power tests all were within normal limits. Electrocardiogram showed left ventricular preponderance.

Blood bromide level on July 6 was 144 mg. per cent. An electroencephalogram on that day was reported as "a markedly abnormal record, which from a background of generalized slowing, shows multiple focal concentrations which are more common in the anterior half of the cortex, especially on the left."

From July 7 to July 11, 2,000 cc. of normal saline were given intravenously, daily. She became progressively more alert and rational. On July 12, a second electroencephalogram was reported as showing "marked improvement with only minimal amount of frontal slowing." This tends to confirm a toxic encephalopathy in the clearing up process. The blood bromide level, which had dropped to 133 mg. per cent, had decreased further to 85 mg. per cent. On July 16, the day she was discharged, she was rational and oriented. There was a residual minimal aphasia and perseveration. She walked with a slight, right limp.

Comment. There are about 5 gr. each of ammonium, potassium, and sodium bromide[10] in every dram of elixir triple bromides. Assuming the 16 oz. prescribed to be the total consumption, the dram three times a day for 30 days would not exceed

* A more accurate picture of the over-all incidence of bromide intoxication was found at the Los Angeles County Hospital where 100 persons with bromism were admitted between 1949 and 1951. Ten of them were on a low-sodium regimen.

the 3 Gm. of bromide recommended as the therapeutic dose for the normal individual on an unrestricted sodium-chloride intake. In this individual, however, the reduction of the chloride apparently contributed to the toxic effect of a seemingly safe dose of bromide. The changes in personality and behavior cleared up as the bromide blood level fell after the administration of chloride. The residual electroencephalographic findings, right Oppenheim, and favoring of the right leg could have been on the basis of a small cerebrovascular accident in the left motor area.

Case II. A 47 year old shoe manufacturer was admitted to the hospital on December 16, 1947, in a semicomatose state with a diagnosis of hypertension and incipient uremia. According to his wife, he had consumed half a large bottle of bromoseltzer in less than an hour the night before. She did not know how much more he had taken, but the following morning when she tried to awaken him he could not talk intelligently or stand upright. For the past several years he had high blood pressure and asthmatic attacks and had taken sometimes as many as three large bottles of bromoseltzer a day for his headaches. He had been placed on a low-salt diet. His lips and finger nails frequently looked blue; this was most marked after a severe paroxysm of coughing. Physical examination revealed a confused cyanotic, lethargic, emphysematous man in marked respiratory distress with blood pressure of 240/100. There were loud inspiratory and expiratory wheezes scattered throughout both lung fields. His heart sounds were distant. There were a few furuncles on his chest and face. His reflexes were hypoactive throughout. Aminophyllin, administered intravenously, partially improved his breathing and diminished the cyanosis somewhat. Complete blood count, urinalysis, and the Kline test revealed no abnormality. X-ray examination of his chest showed left ventricular hypertrophy with slight vascular congestion of the lungs. His NPN was 54, plasma chlorides 528, and bromides 200 mg. per cent.

From December 18 to 20, the patient was given daily doses of 6 Gm. of sodium chloride orally and 1,000 cc. of glucose in normal saline intravenously. On December 20, his plasma chlorides were 545 mg. per cent, bromides 191. On December 22, they were chlorides 4,000, bromides 108 and NPN 32. By December 21, he was markedly improved and his color was better. His sensorium cleared progressively until December 23, when he was discharged from the hospital.

Comment. According to the label, which says it contains 5 gr. of sodium bromide and 2½ gr. of acetanilid per teaspoonful, the large, 12 oz. bottle of bromoseltzer contains 30 Gm. of bromide and 15 Gm. of acetanilid. Thirty grams is considered a toxic dose of sodium bromide which may produce[11] alarming symptoms in an adult whose chloride intake is unrestricted. In the three large bottles, this man was taking 90 Gm. of bromide a day, self prescribed, without medical supervision. The elevated NPN suggests impaired renal excretion which could have augmented the bromide retention. The 45 Gm. of acetanilid could have been a contributory cause of the cyanosis.

Case III. A 54 year old woman was admitted on June 2, 1948, for investigation of pain over the midthoracic spine radiating to the right side, which had persisted for five months following a virus respiratory infection. Her blood pressure had

varied between 200 and 180 for many years, and she had an enlarged heart. Eighteen years previously she had had a nervous breakdown. She was placed on a 400 mg. sodium diet, and two drams of elixir triple bromides were ordered, to be given every three hours as needed for nervousness and excitability. On June 26, bromides were discontinued after 52 dr. had been given. The nurses noted the patient showed an increasing tendency to sleep and a lack of attention. At this time she was found to be sluggish, slow-moving, and slow-thinking. Her speech was slow, and, due to retropulsion, she had difficulty sitting up on the edge of the bed. Her gait was decidedly unsteady even with support. She would call for a bedpan for a bowel movement but occasionally began to be incontinent of urine. Her deep reflexes were easily obtained in the arms but were absent in the lower extremities; the abdominal reflexes were absent. There was marked tenderness over the thoracic spine. On June 27, she fell on the way to the bathroom. At that time she was confused, semi-stuporous, and irrational. She showed perseveration, memory loss, and disorientation for time. She manifested facetiousness and jocosity, which were suggestive of frontal lobe tumor. She began to have visual and auditory hallucinations at night. There was a slight left facial weakness. On June 23, examinations of the spinal fluid showed a pressure of 240 mm. water, protein 126, no cells; and on June 26, examinations showed a pressure of 180, protein 150, and no cells. The Wasserman and Gold curve were negative. An electroencephalogic report said: "from a background of generalized slow wave activity, the anterior third of the cortex showed concentrated abnormality with some left preponderance." On July 2, an air encephalogram done by a neurosurgeon showed increased air in the subarachnoid space and slight dilatation of the left frontal horn. This was interpreted as indicating a certain degree of atrophy of the frontal lobe. Since there was no evidence of a space-taking lesion, the neurosurgeon felt there was no reason to proceed further with burr holes through the skull.

The initial blood bromide was 195 mg. per cent. After sodium chloride therapy, a second electroencephalogram on July 8 was reported as showing "some clearing up in the posterior half of the cortex which could be explained on the basis of progressive detoxication from bromides—this explanation would not suffice to account for the severe abnormality in both frontal areas." The blood bromide level had come down to 141 mg. per cent. After an x-ray of the chest showed marked enlargement of the transverse diameter of the heart shadow to the left, as well as the right, and an electrocardiogram showed the pattern of left-ventricular preponderance, the sodium chloride was changed for ammonium chloride in enteric-coated capsules. As therapy continued, the mental disturbances decreased progressively until the patient became rational and oriented enough to be discharged on July 16. One year later she had a cerebral thrombosis which resulted in a left hemiplegia.

Comment. In this case the bromides were prescribed simultaneously with a markedly restricted sodium-chloride intake. The 52 Gm., taken over a five day period, produced a toxic effect which lasted for three weeks and so confused the clinical picture that an air encephalogram was done, and even burr holes were contemplated to rule out a frontal lobe brain tumor. After chloride therapy was started, the delirious toxic state due to bromide medication subsided. The residual minimal findings were

probably on the basis of arteriosclerosis, since she had a cerebral vascular accident one year later. Because of her cardiac condition, the chloride therapy was changed from sodium to ammonium chloride.

DISCUSSION

Each of the three cases showed evidence of hypertension and vascular disease for which they had been placed on restricted sodium-chloride intake. The disturbance of mentality and aberrations of behavior pattern initially were ascribed to hypertensive encephalopathy in case 1, incipient uremia in case 2, and frontal lobe brain tumor in case 3. That they were toxic, delirious states due to bromide intoxication was completely unsuspected or came as a belated afterthought. After bromide medication was discontinued and chloride therapy was pushed, the blood bromide levels decreased and that part of the clinical picture and the electroencephalographic findings due to bromism cleared up.

In case 1, the patient already had been on a salt-free diet when bromides were prescribed. Conversely the cumulative effect of a dose of bromides, which usually have been well-tolerated by an individual, may produce toxicity rapidly when his sodium-chloride intake is restricted.

Case 2 illustrated that the patient taking a self-prescribed drug for sleep or headache of "nerves" may not know it contains bromides and may take it to excess. He may neglect to inform his doctor who may be prescribing additional bromides. The patient certainly cannot be expected to know that the headache medicine he buys over the counter without a prescription is a potentially harmful bromide made actively so by the dietary chloride restrictions instituted by his unsuspecting doctor. Ten years ago Bucy, Weaver, and Camp[12] described bromide intoxication of unusual severity and chronicity resulting from self medication with bromoseltzer. This was only a year after the hazards of bromidism in proprietary and uncontrolled hypnotic medication had been brought to the attention of the medical profession in an editorial[13] in the *Journal of the American Medical Association*. Recent writers[14-a,b,c,d,e,f] stress the continuing hazard of the easy availability of bromide preparations to the lay public. Even the manufacturer of one of the proprietary products, neurosine,[15] limits its distribution to physicians' prescriptions. Yet, many other products widely advertised as being harmless still are freely sold over the counter. This potential danger has been made an active one now by the widely prevalent use of low-salt diets.

Case 3 illustrates the step by step development of bromide intoxication described by Millikan.[16] The woman first had an increased desire to sleep and later had trouble paying attention. Then slowness of thought and slurring of speech appeared. This was followed by a staggering of the gait. She became so ataxic that she could not stand or walk. After a fall she had to be confined to bed. Then she became semistuporous and incontinent. Hallucinations, mostly visual, appeared and she was disoriented as to time. According to Curran,[17] the hallucinations of bromide psychosis are usually distant from the patient and consist of large objects.

The bulwark of the management of bromide intoxication long has been the ad-

ministration of sodium chloride orally and intravenously in large amounts. This is of course strictly contraindicated for patients in heart failure. The same holds for attempts at refinement of the treatment of bromism by the employment of adrenal cortex extract[18] and desoxycorticosterone[19] to retain sodium chloride in the body.

Cornbleet[20] has suggested that substitution of ammonium chloride for the sodium halide causes a more rapid excretion of the bromide. Bergner,[21] however, has pointed out that an excess of ammonium chloride may itself produce drowsiness and mental confusion, which are prominent symptoms of bromide intoxication.

Cation exchange resins[22] are available which theoretically should be of use in the management of bromism in individuals on restricted sodium intake, since they are directed at the removal of sodium ions without the excretion of the chloride ions. Harris and Derian[23] have done work to show the value of massive doses of niacinamide in the treatment of bromide intoxication. This form of therapy would not be contraindicated in cases of cardiac decompensation.

SUMMARY

Great caution should be exercised in the administration of bromides to patients with congestive heart failure, edema, and hypertension because:

(1) The measures taken to lower body sodium also lower the chloride and thus predispose these patients to bromide intoxication.

(2) If bromism develops, the most effective antidote, massive doses of sodium chloride, are contraindicated because of the underlying cardiovascular disease.

Bromism should be suspected if central nervous symptoms appear in patients whose sodium intake has been restricted or output increased. When the body chloride is sufficiently lowered, usually safe doses of bromide may cause toxic delirious states. Self-administered proprietary products are an unsuspected source of bromides. In the treatment of these patients, the substitution of ammonium for sodium chloride is discussed and the adjuvant use of cation exchange resins which remove sodium without excretion of chloride is suggested.

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Advantages of Oral Diuretic Therapy

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The utility of mercurial diuresis as a measure in the treatment of congestive heart failure has been established for over two decades. In spite of reports by investigators[1–6] describing the effectiveness of oral mercurial diuretics, this method of administration of mercurials has not been well accepted among practicing physicians. The compounds in use hitherto have either been irritating to the gastro-intestinal tract or have fallen short in the desired clinical response.

Because of the fact that the modern treatment of chronic myocardial insufficiency has been improved by better understanding of digitalization, the use of low sodium diet and at times anticoagulant therapy, together with other measures including elimination of total bed rest in favor of a program of restricted activity, more patients with evident or potential heart failure remain active in our present social life. Important among the measures of treatment to eliminate excess water in tissues and associated sodium retention, which may occur in the ambulatory cardiac, is mercurial diuresis. Parenteral administration of mercurial compounds for this purpose remains the most effective route of therapy, but it does appear that there is a place in the cardiac regimen for an effective oral mercurial diuretic. Results with Neohydrin* in a group of ambulant cardiac patients seen largely in office practice seem to indicate that this drug is useful both from the standpoint of convenience to the patient, as well as therapeutic efficiency.

In comparison study of diuretic response in human subjects, Greiner, Gold and co-workers[7] found that oral mercuhydrin was one twenty-fourth as effective as the same parenteral preparation; in the case of the thiol compound studied, the oral response was one eleventh of the parenteral; for neohydrin the oral drug was one fourth as efficient as the parenteral. In further comparisons,[7] Greiner and Gold found neohydrin to be about four times as efficient as mercuhydrin using the parenteral route. In dog assay experiments the same degree of increased diuretics was shown, neohydrin over mercuhydrin.

Orally administered mercury compounds in the past have probably afforded only limited absorption and therefore have had a suboptimal effect upon the mechanism of diuresis, the renal tubule. Neohydrin has been shown to be absorbed relatively well. Mercury excretion studies in dogs, given comparable amounts orally of mercuhydrin and neohydrin, showed approximately twice as much mercury in the urine sixteen hours after neohydrin as mercuhydrin.[8] Toxicity experiments in dogs prove that neohydrin is approximately in the same range as mercuhydrin. As far

*Neohydrin, 3-chloromercuri-2-methoxypropylurea, manufactured by Lakeside Laboratories, containing 10 milligrams of mercury per tablet.

as certain cardiotoxic effects are concerned (QRS changes), neohydrin has less toxic properties than mercuhydrin.

During the past 18 months, 92 patients with chronic congestive heart failure have been given neohydrin for varying periods of time in order to control better excess fluid retention. It was the purpose of this trial with an oral diuretic to evaluate the clinical effectiveness of neohydrin in office practice for the treatment of congestive cardiac failure. All but two of these patients were ambulatory to the extent of being seen in the office. The degree of cardiac impairment was sufficient in all to necessitate periodic administration of mercurial diuretics in addition to digitalis and adherence to a low sodium diet. In many cases adjuvant therapy such as cation exchange resins and/or ammonium chloride had been used. Neohydrin was employed in the regimen of all patients and, in many, replaced resins and/or ammonium chloride. The measure of success contributed by neohydrin could be fairly accurately shown clinically by better edema control, thus necessitating lessened, or in some cases, no further injections of a mercurial diuretic.

Approximately one tenth of the total number were already taking other oral mercurial diuretic compounds with varying results. In all patients of this group, neohydrin has been shown to maintain better diuretic efficiency. Longer intervals between supplementary parenteral mercurial injections were observed in the more severe cases of congestive failure. Daily weight records were kept by all these patients in whom oral mercurials had been given as a maintenance diuretic therapy. No intolerance to this form of mercurial drug was encountered in the patients. It thus appeared evident in a relatively small group of patients previously judged to be benefited by oral mercurial diuretic therapy that replacement by this new compound offered an advantage in treatment.

In the majority of patients encountered in a state of congestive failure, parenteral mercurials were administered to effect initial diuresis in conjunction with other methods of treatment, including rest, digitalization, and sodium restriction in diet. Those patients, who required continuing therapeutic fluid and sodium-depleting efforts after becoming ambulant, were given neohydrin. The dosage was regulated according to the apparent need for diuresis. In practically all persons the dosage had to be varied over a period of time because of the very nature of their heart disease and additional factors affecting their cardiac status. For approximately 14 months, divided oral dosage has been extended to 5 tablets daily in the more severe cases. In 4 patients, where three tablets daily gave inadequate or even poor results, higher dose levels of 2 tablets after breakfast and lunch and 1 tablet after dinner improved the diuretic therapy. So far, no patients who tolerated 3 tablets per day have shown side effects with a higher dose level up to 5 tablets daily.

The opinion has been reached that in milder cases of chronic congestive failure it is better to prescribe 2 tablets on alternate days or even at weekly intervals, than it is to continue with a dosage of 1 tablet per day. Diuretic responsiveness is apparently enhanced when there is a periodic higher level of absorbed mercurial compound, rather than a minimal amount of drug continually present in the body. The experience in milder degrees of edema leads one to hold to the concept that a

necessary threshold level of mercurial diuretic in the body is necessary for efficient diuresis.

Initially each patient was given an adequate complete physical examination including cardiac fluoroscopy, electrocardiogram, complete blood count, urinalysis, and other pertinent diagnostic aids. All individuals were instructed to weigh daily and to report noteworthy changes in their progress. Return visits were regulated according to the need and practicability to allow necessary control of dose and to evaluate the response to maintenance therapy with an oral mercurial diuretic, or to use supplementary diuretic measures when necessary. Progress examinations of blood and urine were carried out in all cases after long intervals on this drug.

All patients were instructed to adhere to a low sodium diet. The diets used approximately 20 mg. of sodium in the most severe cases and either 400 or 800 mg. of sodium in the less severe cases. Daily orange juice was included to obviate the possibility of potassium depletion. In a number of patients suggestions were made for temporary increased neohydrin dosage in order to anticipate or offset lapses in the low sodium diet necessitated by travel or social engagements. In order to prevent sodium depletion the dosage of mercurial was either decreased or administered at less frequent intervals whenever patients showed a tendency toward maintaining better edema control. In three instances temporary mild hyponatremia was suspected because of the clinical picture. Addition of salt to the diet promptly relieved the symptoms and thereafter the mercurial dose was decreased.

It must be clearly stated that mercurial diuretics, either orally or parenteral, were used to combat water retention indicated by weight records, clinical observation for edema, and paroxysmal nocturnal dyspnea.

There appeared to be no significant difference in the effectiveness of oral mercurials in different types of heart disease. In most patients 2 or 3 tablets on alternate days afforded satisfactory diuretic control. Occasional injections of parenteral drugs were necessary in more severe cases of fluid retention. When the maximum dose of 5 tablets daily was inadequate as it was in 4 patients, even with sodium restriction, oral therapy was omitted in favor of parenteral injections two or three days per week. It must be added that in these very refractory cases of edema, oral mercurials proved more satisfactory in combatting fluid retention than acidifying salts or resins. In tabulating results in patients in congestive failure, such a result with neohydrin, that is, its use between parenteral injections, was classed as an unsatisfactory response. In 3 of these most severe cases, neohydrin on this basis has been continued over a period of a year and a half except for periods of trial with other edema-combatting measures.

Most patients maintained a relatively edema-free state by way of a smooth, nondrastic diuresis, thus obviating otherwise more frequent parenteral injections and/or more complicated adjuvant oral diuretics, and the improvement was evident to observer and patient. Approximately 80 per cent of the patients followed for three months or longer had either good or excellent results with neohydrin therapy.

Nausea and vomiting were not encountered as objectionable symptoms attributable to neohydrin. In several patients this condition cleared after compensation was

restored and continued oral mercurial dosage was uneventful. Mild diarrhea was noted in 4 patients, but this did not lead to interruption of therapy. Two elderly women with congestive failure developed a scaly, reddish, maculopapular rash over the extremities during therapy which cleared when the drug was stopped. In one patient with noncardiac edema, stomatitis necessitated discontinuance of the drug after four months' treatment. Three cases of hyponatremia diagnosed clinically were encountered.

Of the 92 patients who have been given neohydrin for the past year and a half, 11 have succumbed of heart disease. In 6 cases, necropsy study of the liver, kidneys, and heart failed to disclose toxic changes from mercury in these organs.

In summary, neohydrin appears to offer a number of advantages as an oral diuretic in the control of fluid retention in chronic myocardial insufficiency. It has a relatively high efficiency in respect to mercury content when oral compounds are compared to parenteral products. Maintenance oral mercurial diuretic therapy under proper direction offers an opportunity to simplify the cardiac regimen by lessening or in some cases replacing the need for injections of mercurials. While it does not appear that parenteral mercury diuretics will be replaced by this drug or by others such as recently introduced Cumertilin,* it does seem that further utilization of these oral preparations will add to the therapy of heart disease. Higher oral dose levels may be adopted in the future according to the work of other observers.[9]

CONCLUSIONS

1. A new oral mercurial diuretic (neohydrin) has been proved by previous animal and clinical experiments to offer advantages over older nonparenteral mercurials.

2. Excellent or good results were obtained in 80 per cent of the ambulatory patients followed for three months or longer.

3. Neohydrin as an oral diuretic provides considerable economic advantages to the patient in reducing the need for more frequent office visits.

4. The dose of neohydrin can be conveniently increased to meet changes in the sodium intake of patients during travel.

5. Simplification of the decompensated cardiac's regimen by providing for maintenance oral mercurial therapy results in a smoother, more continuous diuresis than with parenteral drugs.

6. Oral mercurial therapy may in many cases replace cation resin and/or salt therapy.

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*Manufactured by Endo Products, Inc.

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Neohydrin*
A New Oral Mercurial Diuretic†

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Numerous organic mercurials have been introduced for diuretic therapy and at present can be used intravenously, intramuscularly, subcutaneously, rectally, or orally. Although merbaphen, the first mercurial diuretic to be used extensively, was administered intramuscularly, it was modified for intravenous use and served as the principal diuretic drug for more than two decades.[1] Quest for a less toxic preparation led to the development of a urea succinyl mercurial theophylline combination (meralluride), which could be given intramuscularly, and to mercaptomerin sodium (thiomerin), which could be given subcutaneously. Many attempts have been made to develop a suitable oral preparation. Calomel was used prior to the era of organic mercurials, but severe catharsis and uncertainty of intestinal absorption precluded effective diuresis in most instances. The combination of mersalyl and theophylline was used by some workers but led to a high incidence of gastrointestinal reactions.[2] This was followed by oral meralluride,[3] and recently, an allyl-urea type of mercurial, neohydrin.[4]

This is a report of clinical experiences with the latter preparation in ambulatory patients.

PHARMACOLOGY

The efficacy of mercury as a diuretic depends on the amount which reaches the kidney, its activity depending on depression of chloride resorption in the tubules.[5] Radioactive studies of meralluride reveal that approximately 60 per cent of intravenously administered mercury can be recovered in the urine, whereas only 5 per cent of mercury given by mouth finds its way into the urine.[6] Most of the oral preparation is not absorbed and passes into the stools with a resultant systemic to oral potency ratio of 12:1.

An attempt has been made to modify an organic mercurial so that its tolerance is good and the systemic to oral potency is low. Preparations with a high ratio are of little value therapeutically, since too much material would be required and the incidence of toxicity would be high. Clinical studies have suggested a 4:1 oral: systemic ratio for neohydrin.[7] With this ratio, an average patient requiring 40 mg. of mercury in the form of 1 cc. of meralluride intramuscularly should require 160 mg. of mercury in the form of neohydrin. Neohydrin tablets contain 10 mg. of mercury. Thus 16 tablets would theoretically be necessary to provide a diuresis equivalent to 1 cc. of meralluride.

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*Supplied by Lakeside Laboratories, Inc.

†From a research project at the Cardiac Clinic, Department of Medicine, Jersey City Medical Center.

DIURETIC CAPABILITIES

Selection of a diuretic agent should be based on time of onset of action, the degree of diuresis, and the duration of activity. An ideal diuretic in an emergency should produce a rapid diuresis of short duration. On the other hand, an agent for maintenance therapy may have a latent period but should provoke a diuresis of relatively long duration. Systemic mercurials are currently the preparations of choice where speed is demanded, but they are often undesirable when slow, smaller diuretic effects are wanted. Comparative studies of the commonly available mercurial preparations indicate neohydrin to be the best type of agent in ambulatory patients requiring periodic mercurials (table 1). Although it has the potential of evoking a major diuresis in some patients, this is rare. The degree of diuretic effect obtained with neohydrin is directly related to the dosage employed, and its greatest efficacy is in providing a slow maintained diuresis which minimizes the possibility of any acute disturbances in fluid and electrolyte balance (fig. 1).

A study of 32 ambulatory patients in chronic congestive failure revealed neohydrin could be used to replace systemic mercurials in 25 patients (78 per cent). These patients were previously maintained on 1 to 12 cc. of parenteral mercurials weekly, over a period of 1 to 8 years prior to the use of this oral preparation. There were 15 males and 17 females, ranging in age from 30 to 77 years. Fourteen patients had

TABLE 1

Effects of Currently Available Mercurial Diuretics

Drug	Route of Administration	Diuresis	Comment
Mercupurin	Intravenous	Good diuresis beginning in one half hour with maximum in less than four hours.	Rapid diuresis, but occasional sudden deaths have been reported.
Mercuhydrin	Intramuscular	Large diuresis beginning in two to three hours lasting 12 hours.	No sudden deaths, good diuretic effect. Occasional local reactions and some cases of excessive diuresis.
Thiomerin	Subcutaneous	Large diuresis beginning in one and three-quarter hours and lasting over 10 hours.	Can be self-administered, rapid diuresis. Occasional local reactions and some cases of excessive diuresis.
Neohydrin	Oral	Gradual diuresis lasting up to 24 hours.	Ease of administration, a few gastrointestinal reactions, moderate diuresis.
Mercuhydrin	Rectal	Gradual diuresis lasting over 24 hours.	Has advantage of ease of administration but marked local reactions occur and diuretic effect is variable.

hypertensive heart disease, 10 rheumatic heart disease, 2 arteriosclerotic heart disease, and 1 chronic cor pulmonale. Each of the patients had either Grade II or Grade III heart failure (American Heart Association classification). The effectiveness of neohydrin was determined by changes in weight and symptoms over a 52 week period.

During the first week of treatment, there was a decrease in weight in 22 patients (68.8 per cent), an increase in 7 (21.9 per cent), and no change in 3 (9.3 per cent). (Table II.) A comparison of continuous administration of neohydrin with its in-

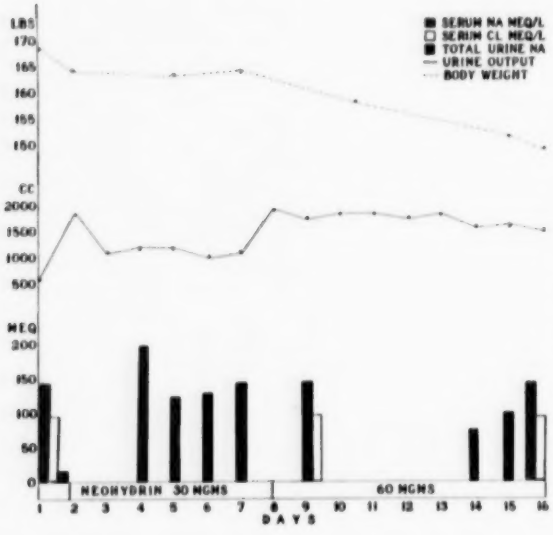

FIG. 1. Findings in a 66 year old male with arteriosclerotic heart disease in congestive failure treated with daily doses of neohydrin. Note steady moderate diuretic effect with little change in serum sodium.

terrupted use revealed no significant difference in total effect or toxicity. Continuous administration provided a smoother diuresis with fewer fluctuations.

Wherever possible, an attempt was made to provide an amount of mercury by mouth which would approximate the amount previously received. Patients who had required 1 to 3 cc. of parenteral mercurials per week were found in general to respond excellently to from 1 to 3 tablets of neohydrin daily (table III). Results were judged as excellent if evidences of fluid retention, such as dyspnea, ankle edema, became less troublesome; good if there was no change, and unsatisfactory if the patient became worse. Twelve patients (37.5 per cent) had excellent clinical responses, 13 (40.5 per cent) good responses, and 7 (21.9 per cent) unsatisfactory responses. Unsatisfactory responses occurred mainly in patients who required more than 4 cc. of parenteral diuretics weekly.

Type of heart disease, duration of heart failure, age, and sex had no influence on the response to neohydrin. Failure to adhere to diet, digitalis toxicity, infection, and excessive physical activity were associated with extra fluid accumulation de-

TABLE II

Weight Changes in Patients During First Week of Therapy

No. of Patients	Weight Change	Per Cent of Patients
2	11–14 lbs. lost	
5	7–10 lbs. lost	
9	3–6 lbs. lost	68.8%
6	less than 2 lbs. lost	
3	no change in weight	9.3%
7	increase in weight	21.9%

spite continuation of neohydrin. However, transient increases in fluid accumulation did not necessitate the use of parenteral mercurials in any of the patients.

The chief advantages to the patient consisted in a discontinuance of injections and absence of copious diuresis, which was often debilitating and productive of symptoms. Disadvantages were primarily related to inability to effect an adequate diuresis in 7 patients who required a larger amount of mercury than was supplied by their neohydrin.

TOXICITY

Gastrointestinal reactions are the most frequently encountered side effects from oral mercurials. These reactions are probably related to chemical transfer of organic mercury from the lumen of the bowel to the capillaries. Since mercury is a protein precipitant, irritation of the intestinal mucosa is inevitable. Enteric coating of the organic mercurial lessens the degree of irritation by selecting the area for absorption, but decreases the amount of mercury absorbed. Increase in dosage is usually accompanied by an increase in gastrointestinal reactions. The incidence of reaction

TABLE III

Response to Neohydrin in Comparison to Previous Requirement of Parenteral Mercury

No. of Patients	Previous Requirement of Parenteral Mercury per week	Patients Responding to Neohydrin No	%	Daily Dosage of Neohydrin
4	1 cc. (40 mg. Hg)	4	100	1–3 Tablets
6	2 cc. (80 mg. Hg)	6	100	
3	3 cc. (120 mg. Hg)	3	100	
10	4 cc. (160 mg. Hg)	7	70	3–6 Tablets
7	6 cc. (240 mg. Hg)	4	57	
2	12 cc. (480 mg. Hg)	1	50	

to neohydrin has varied from 5 per cent to 28 per cent,[4-8] the higher per cent occurring in patients on doses of 60 to 80 mg. daily. In the authors' experience, 3 patients (12 per cent) had gastrointestinal reactions consisting of vomiting in one, abdominal pain in one and diarrhea in one. Gingivitis, stomatitis, and mercurial deposits in the oral cavity were noted in one patient receiving large doses of neohydrin but appeared to be related to poor oral hygiene. Systemic reactions to mercurial diuretics were not observed with oral preparations. The incidence of excessive diuresis with salt depletion, muscle cramps, and marked lassitude is reduced because of slower reaction. One patient in our series who developed a skin eruption with various parenteral mercurials had no such reaction with neohydrin. No serious evidences of mercurialism have been reported with neohydrin.

SUMMARY

The clinical need for an effective oral diuretic can be partly met by neohydrin, a new allyl urea type of mercurial. This drug has a low systemic to oral potency ratio, representing an improvement over other available preparations. It provided an adequate diuresis in 78 per cent of 32 ambulatory cardiac patients, being most useful in those patients who required 1 to 3 cc. of a parenteral mercurial each week. Its greatest value was in maintaining patients requiring small doses of parenteral mercury regularly. The incidence of gastrointestinal reactions was low but increased with larger doses. Few patients (9.3 per cent) required discontinuance of therapy because of these reactions.

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Electrolyte Disturbances Associated with Mercurial Diuretic Therapy in Congestive Heart Failure

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Mercurial diuretic therapy in congestive heart failure may result in severe electrolyte imbalances. The widespread use of these drugs today renders such imbalances of considerable clinical import. These disorders are, for the most part, readily amenable to proper therapy, but they are not infrequently mistaken for intractable complications of congestive heart failure. The purpose of this paper is to facilitate recognition of the individual deficiency states, to indicate some of the pathophysiology involved, and to emphasize the need for specific replacement therapy.

The effect of a mercurial-induced diuresis on the electrolyte content of the body fluids depends, of course, upon the amount of water and of the various electrolytes lost in the urine. In cases of congestive heart failure, the usual response is such that physiologic proportions remain within the body. Under certain circumstances, however, disproportionate losses occur, and the resultant imbalance may conform to one or three recognizable patterns, namely, (1) hypochloremic, hypopotassemic alkalosis, (2) salt depletion with hypovolemia, or (3) salt depletion with hypervolemia.

Hypochloremic Alkalosis: Schwartz and Wallace observed that during mercurial diuresis some individuals show disproportionately large amounts of potassium and chloride in the urine.[1] This may result from the administration of excessive amounts of the diuretic, but may also represent hypersensitivity to the drug, as it commonly occurs following only one or two injections.

The syndrome usually develops from three to seven days after the institution of mercurial diuretic therapy. The patient loses weight rapidly and becomes dehydrated. Anorexia develops and is followed by weakness and periods of confusion. Renal failure is progressive and leads to coma and finally death. Though an occasional patient may proceed rapidly to such termination, the usual patient becomes relatively refractory to the mercurial agent as alkalosis develops.

On examination patients having hypochloremic alkalosis reveal evidences of extracellular fluid deficit. The tongue and mucous membranes are dry, and the skin is found to have lost its elasticity. Manifestations of tetany may be present, but more often this is of the latent type and is only elicited by muscular stimulation. However, the administration of potassium-containing fluids, without additional calcium, may lead to tetany.[2]

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The serum bicarbonate is elevated, and the serum chloride may reach very low levels. There is elevation of the hematocrit and usually of the serum sodium concentration. The serum potassium may actually be normal or only slightly decreased due to hemoconcentration, but dilution by the administration of potassium-free fluids will promptly expose the underlying, absolute deficiency. The latter is unquestionably more marked in the intracellular compartment, inasmuch as it has been shown that in alkalotic states a considerable portion of the intracellular potassium is replaced by sodium. Likewise, in alkalosis, clinical symptoms of potassium deficiency occur more readily because of the physiologic antagonism of the sodium and potassium ions. Such clinical antagonism has repeatedly been observed, and experimental lesions produced by potassium deficiency can be accentuated by the administration of excessive sodium.[2]

Serum calcium concentration may be diminished, but it is usually within the range of normal values. However, in alkalotic states the concentration of ionized calcium is reduced, and it is likely that there would occur more manifestations of neuromuscular irritability if it were not for the proportional decrease in potassium ions. Derangement of the normal potassium-calcium ratio is apparently a *sine qua non* for the development of clinical tetany. (Table I.)

TABLE I

Electrolyte Patterns in Patients with Potassium Deficiency Accompanying Hypochloremic Alkalosis after Mercurial Diuretic Therapy of Congestive Failure

Serum Concentrations

	Sodium (mEq/l)	Potassium (mEq/l)	Calcium (mEq/l)	Chloride (mEq/l)	CO_2 (HCO_3 mEq/l)	BUN (Mg. %)	Hematocrit (Vol. %)
Case 1	149.7	4.1	5.4	80	40	46	68
Case 2	147.1	3.9	4.9	72	42	50	75
Case 3	150.1	4.0	3.9	82	46	36	70
Case 4	149.0	3.6	5.2	76.5	50	101	72
Case 5	146.2	3.9	5.0	80	70	79	60

Treatment of hypochloremic, hypopotassemic alkalosis is primarily one of replacing the deficient potassium and chloride ions. Calcium should be supplied where clinically indicated. Administration of potassium-containing fluids will result in elevation of the intracellular potassium concentration, together with a return to normal of the extracellular concentration. Renal function is restored, and the alkalosis is readily dissipated. It can readily be seen that if these individuals were treated with sodium-containing parenteral solutions alone, the potassium loss would be augmented, and large amounts of sodium would be retained in the cells. Under such circumstances *intracellular edema* may result.

The hypochloremic alkalosis syndrome may at times be difficult to distinguish clinically from the salt depletion syndrome. However, there are differential findings in each, and recognition should not be long delayed. (Tables II and III.)

TABLE II

Serum Electrolyte Concentrations Illustrative of Differences Associated with Hypochloremic Alkalosis and Those of Low Salt Syndrome

Syndrome	Serum Concentrations: Sodium (mEq/l)	Potassium (mEq/l)	Chloride (mEq/l)	CO_2 (HCO_3 mEq/l)	BUN (Mg. %)	Hematocrit (Vol. %)
Low Chloride						
Alkalosis	150.1	3.0	78.8	48	100	68
Low Salt						
Hypovolemic	132.5	5.6	76	20	146	60
Hypervolemic	121	8.6	70	10	189	21

TABLE III

Clinical Findings Illustrative of the Differences Associated with Hypochloremic Alkalosis as Compared with Those Found in the Low Salt Syndrome

	Hypochloremic Alkalosis	Salt Depletion Syndrome
Occurrence	Fairly frequent	Rare
Onset	Acute	Subacute or chronic
Amount of Mercurial	Usually small	Usually large
Underlying Renal Disease	No influence	Marked predisposing influence
Length of Therapy	Short term	Prolonged
Occurrence of Tetany	Occasional	None

The Salt Depletion Syndrome: This syndrome appears to be a result of the excessive loss of sodium chloride from the extracellular fluid. Fortunately, this does not commonly occur, but it is easily recognizable and prompt remedial therapy may be lifesaving.

For the most part this syndrome occurs in the elderly group of patients subjected to prolonged treatment with the mercurial diuretics, especially those individuals who have had dietary salt restriction as well. The frequency of occurrence of this entity during the summer months leads one to suspect that added salt loss in the sweat may be a contributing factor.

Renal disease appears to be an underlying prerequisite of this deficiency syndrome. Apparently the renal tubular epithelium has lost some of its normal function, that of conserving base and manufacturing ammonium. The additive effect of the mercurial diuretic on the already damaged tubular ionic transport mechanism results in excessive loss of electrolytes from the plasma.

In patients with *hypovolemic low salt syndrome*, the peripheral blood shows hemoconcentration, and the plasma proteins are usually found to be elevated.[4] Serum chloride and sodium values may be normal or only slightly lowered. The cardiac output falls, and the glomerular blood flow is reduced. Peripheral resistance may

be elevated, probably as a compensatory mechanism to assure adequate blood supply to vital organs. The concentration of urea rises in the blood and practically disappears from the urine. (Table IV.)

TABLE IV
Electrolyte Patterns in Patients with Low Salt Syndrome with Hypovolemia
Serum Concentrations

	Sodium (mEq/l)	Potassium (mEq/l)	Chloride (mEq/l)	CO_2 (HCO_3 mEq/l)	BUN (Mg. %)	Hematocrit (Vol. %)
Case 1	138.2	6.8	72	10	110	64
Case 2	132.5	5.6	78	20	152	68
Case 3	136	5.0	70	18	168	60

The clinical picture of this syndrome is similar to that seen in patients with adrenal cortical insufficiency. Early in the complex, apathy, lassitude, and lethargy become manifest. Progressive anorexia ensues, accompanied by nausea and vomiting. Cramps in the abdomen and large muscle groups may be a prominent feature. Uremia commonly occurs and is often the presenting symptom. In these patients physical examination reveals evidences of dehydration. The tongue and skin are dry, and the skin is inelastic.

Therapy consists of replacing the extra cellular fluid and electrolyte deficit as rapidly as possible. The parenteral administration of 500 to 1000 cc. of 3 to 5 per cent salt solutions will usually result in rapid clinical improvement. Fifty to 75 Gm. of salt are at times necessary to replace the deficit. Supplementing parenteral therapy with orally administered salt may accelerate correction of the deficit.

TABLE V
Electrolyte Patterns in Patients with Low Salt Syndrome and Hypervolemia
Serum Concentrations

	Sodium (mEq/l)	Potassium (mEq/l)	Chloride (mEq/l)	CO_2 (HCO_3 mEq/l)	BUN (Mg. %)	Hematocrit (Vol. %)
Case 1	122.5	8.2	87	10	180	28
Case 2	118.8	9.6	76	10	260	20
Case 3	128	5.6	72	12	150	32

In patients with a *hypervolemic low salt syndrome*, the changes in the circulating blood are found to be quite different from those found in the hypovolemic state.[5] There is no evidence of hemoconcentration. The serum sodium and chloride values may reach very low levels. (Table V.) The extracellular spaces become engorged with electrolyte-poor fluid. Edema increases and renal failure is apparent.

These patients also present symptoms of lassitude, apathy, anorexia, nausea, and renal failure. In addition they have static or increasing edema, despite, in many cases, the use of increasingly large amounts of mercurial diuretics.

The paradoxical phenomenon of increasing edema after salt depletion has been explained on the basis that the mechanism which initiates maximal reabsorption of sodium by the renal tubule also promotes maximal water reabsorption, and this may occur when there is little salt left to be reabsorbed. It is probable that this condition has often been attributed in the past to "intractable heart failure."

Hyperpotassemia is commonly found accompanying the low salt syndrome. The failure of the renal mechanism to maintain adequate urinary output results in retention of abnormal amounts of this potentially toxic ion. The associated protein catabolism releases large amounts of intracellular potassium into the body fluids, augmenting the steadily increasing concentration of this cation in the extracellular fluid. The concomitantly existing low serum sodium concentration augments the physiologic action of the potassium, and symptoms of potassium intoxication may occur at only slightly elevated serum potassium levels. Death is usually the result of the toxic effect of the potassium on the heart.

Fortunately, this syndrome does not occur very often, but when it does it should be promptly recognized and treated with large doses of parenterally administered salt. Usually diuresis promptly ensues. However, if this syndrome is allowed to progress, the body becomes more and more engorged with salt-poor fluid, and reversal of the electrolyte imbalance becomes more difficult.

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The Differential Diagnosis Between Cardiac and Bronchial Asthma

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The word asthma was first used by Hippocrates to denote "hurried breathing," and for some time it was considered synonymous with shortness of breath. In 1819 Laennec, the discoverer of auscultation, originated the concept that asthma is distinct from shortness of breath and represents a definite entity characterized by paroxysmal dyspnea without demonstrable associated organic lesions. In 1832, however, Hope[1] called attention to the fact that there are several varieties of asthma, of which organic disease of the heart constitutes one, and that in all instances bronchospasm exists. He recognized the difficulty of distinguishing the asthma produced by disease of the lungs from that due to heart ailments and coined the term cardiac asthma for the latter. Subsequently, cardiac asthma became known as a distinct clinical state. In 1897 Osler[2] described this syndrome so clearly that to date all writers on the subject quote him verbatim.

A severe paroxysm of cardiac asthma is an extremely terrifying experience, since it occurs most often in the middle of the night, generally during the first few hours after the patient has fallen asleep. With this sudden awakening, there is a sensation of anxiety, precordial distress, and suffocation. The patient sits up in bed, grasping the edges to aid the accessory muscles of respiration by fixing the shoulder girdle, and drops his legs over the sides. Frequently the sufferer springs to his feet to open the window in order to relieve his terrible air hunger. On physical examination, a cold sweat is apparent over the entire body, and the skin may be ashen or cyanotic. Cough and expectoration of a foamy blood-tinged sputum is frequently observed. On auscultation, the heart sounds are very rapid, with accentuation of the pulmonic second sound and, at times, an audible arrhythmia is present. The lungs are filled with bubbling râles and numerous rhonchi, and wheezes are heard at a distance.

Bronchial asthma of the allergic type may be defined as a recurrent, paroxysmal dyspnea with cough, expectoration, and wheezing. Such a seizure may likewise occur at night, waking the patient who finds it increasingly difficult to breathe. Although both phases of respiration are accentuated, only the upper part of the thorax appears to be functioning. Particularly characteristic, however, is the difficult, gasping protracted expiration, in the course of which the abdominal muscles become nearly boardlike. On examination, cyanosis is not infrequently present, the respiratory rate is accelerated and the heart rate increased. The pulmonary signs of bubbling, sonorous, and sibilant râles, with wheezes and rhonchi, often obscure the cardiac sounds. The patient assumes a characteristic posture permitting the acces-

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sory muscles of respiration to assist in attempting to overcome the air hunger.

How closely these two clinical pictures resemble each other, and how difficult it often is to differentiate one from the other by physical examination! This is especially so in the older age group, where hypertensive and arteriosclerotic heart disease are common complications. The coexistence of cardiovascular disease and bronchial asthma is by no means rare and, inasmuch as dyspnea, cough, air hunger, and wheezing are features common to both, the problem becomes more perplexing.

Cardiac asthma is synonymous with left ventricular failure and occurs most often in hypertension, lesions of the aortic valve, and arteriosclerotic heart disease. It may, at times, present itself in subjects with mitral stenosis, but in such subjects the attacks are solely the result of an increase in the inflow load without coexisting functional changes in the heart itself. These attacks commonly follow unusually strenuous exertion and rarely occur at night. Recent investigators have demonstrated that exercise produces pulmonary edema only in patients with mitral stenosis who have an increase in resting pulmonary capillary pressures.

Several theories have been advanced to explain the pathogenesis of cardiac asthma, namely (1) back pressure, (2) insufficient aeration, (3) water-shift, and (4) neurogenic or reflex factors.[3]

James Hope[1] was the first advocate of the back-pressure or left ventricular failure concept. He believed that disease of the left ventricle results in an increase in the volume of blood within it, causing obstruction to the transmission of auricular blood which is sufficient to produce back pressure to the lungs resulting in engorgement, dyspnea, and edema. Traube[4] postulated that cardiac dyspnea is due to pulmonary congestion, which causes the capillaries to encroach on the air spaces, thus leading to defective aeration of the blood. The water-shift theory was championed by Brunn,[5] who thought that cardiac asthma is due to a disturbance in water regulation, leading to a passage of fluid from the tissues into the blood stream during the night. The neurogenic or reflex hypothesis stems from the fact that pulmonary edema is often seen in patients with cerebral hemorrhage, tumors of the brain, and other disorders of the central nervous system.

Whatever the mechanism, the outstanding manifestation of cardiac asthma is dyspnea, and the most important factor responsible is pulmonary congestion. Now, in the acute phase of bronchial asthma, the predominant symptom is also dyspnea. In this clinical state it is due to bronchial and particularly bronchiolar obstruction throughout both lungs brought about by the underlying pathology—namely, bronchial spasm and edema, with marked increase of the bronchial secretions.

Dyspnea, regardless of its genesis, involves a decrease in maximal breathing capacity or an increase in actual ventilation, which is the minute-volume of air in any given state of rest or exercise. At times the two conditions coexist. Patients with pulmonary disease ordinarily complain of dyspnea when the breathing reserve is less than 65 per cent to 70 per cent of the maximum breathing capacity. In those with cardiac disease the relationship is less constant, and dyspnea sometimes persists even when the breathing reserve is more than 70 per cent of the maximal breathing capacity. This may be explained by the fact that the muscles involved in ventilation become fatigued as a result of inadequate circulation or anoxia.

Since the physiologic abnormalities in cardiac disease are in many respects different from those in pulmonary disease, various tests have been proposed in an attempt to differentiate one type of dyspnea from the other. Measurements of the total capacity of the lungs and its subdivisions, the partial pressure of carbon dioxide in the arterial blood, the oxygen saturation of the arterial blood, the determination of the cardiac output and of the oxygen intake during a standard exercise test are procedures that offer some clue.[6] During an acute paroxysm, however, such laboratory explorations are much too difficult to perform and, at best, require a complicated setup.

Wheezing is another prominent and characteristic sign common to both conditions. Its mechanism is by no means a settled question. Heyer[7] recorded the respiratory curves of patients with cardiac asthma and demonstrated that they are identical with those of subjects with bronchial asthma. In both types of cases the expiration was prolonged, thus indicating evidence of obstruction of the bronchial tree. Several possibilities have been suggested to explain the presence of wheezing in cardiac asthma, namely, (1) congestion or edema of the bronchiolar mucosa, (2) active bronchoconstriction, (3) compression of the bronchioles by congested capillaries, and (4) intrinsic obstruction due to edema fluid in the bronchiolar lumina. In addition, there may be many unknown contributing factors responsible for the production of wheezes in cardiac asthma.

In order to determine the cause of the clinical syndrome of paroxysmal cough, dyspnea, and wheezing, the history is of inestimable value. Obviously, an attack that follows exposure to a definite allergen or one that is known to occur at frequent intervals in association with an infection in persons below the age of forty strongly suggests bronchial asthma. An additional family history of allergy or the existence of a coexisting disease of hypersensitivity supports this diagnosis. Positive skin tests and the presence of eosinophilia either in the bronchial secretions or in the blood stream confirm its presence. Yet there are a number of elderly individuals who suddenly develop an acute bout of bronchial asthma without previously manifesting signs of any allergic disorder. Demonstration of cardiac enlargement either by percussion or roentgen examination or both, hypertension, the existence of cardiac murmurs, and electrocardiographic evidences of either myocardial damage or conduction disturbances point in the direction of a cardiac etiology. A high incidence of coronary artery disease, hypertension, and bundle branch block with premature beats and gallop rhythm have been reported by many observers in cardiac asthma. When the two conditions exist simultaneously, however, the above criteria are not always very helpful.

The circulation time, which is in inverse proportion to the velocity of blood flow, has been frequently employed to differentiate cardiac bronchial asthma. Considerable importance has been attached to this laboratory finding by Ungar,[8] Plotz,[9] Miller[10] and others. Many observers have found the circulation time definitely elevated in left ventricular failure but normal in bronchial asthma per se.[11–17] At times, when heart failure complicates or is associated with bronchial asthma, an increase in the circulation time merely indicates the presence of congestive failure but does not necessarily rule out the existence of bronchial asthma. Occasionally,

there may even be a normal circulation time in early left ventricular failure, and often the test cannot be performed at the time most needed.

The therapeutic response to various drugs has frequently been employed in the differential diagnosis of certain diseases. The dramatic relief obtained by morphine in congestive heart failure is well known. Morphine breaks the vicious cycle by alleviating the labored breathing, thereby raising the intrathoracic pressure which in turn decreases the inflow to the heart. In addition, morphine relieves the marked apprehension and fear so characteristic of cardiac asthma. In allergic bronchial asthma, on the other hand, the drug may prove extremely dangerous, thus invalidating its potential diagnostic value. In fact, it has even been known to produce immediate death. This may be due to hypersensitivity to the drug itself or to a depression of the coughing reflex, which causes the patient to drown in his own secretions. The author has observed more than one fatality in addicts who administered themselves an increased dose of morphine in an attempt to interrupt an asthmatic seizure.

It has been frequently stressed that the favorable response of bronchospasm to adrenalin connoted an allergic etiology. Inasmuch as Plotz[9] and Heyer[7] have shown that bronchospasm also exists in pulmonary congestion resulting from left ventricular failure, and since Plotz[9] demonstrated that the bronchospasm likewise clears following the use of adrenalin, this concept becomes invalid.

Aminophyllin, through its bronchodilator action, exerts an extremely beneficial effect in bronchial asthma when given intravenously. In cardiac asthma, where bronchospasm is also present, it is equally valuable and relieves the dyspnea in several ways. It increases the vital capacity by relaxing the bronchospasm and improves the force of cardiac contraction by a possible direct effect either on the myocardium or on the coronary vessels. In any case, this drug does tend to lower the venous pressure and shorten the circulation time. Recently, Schuman and Simmons[17] reported no beneficial effects from aminophyllin in cardiac asthma. Their findings are open to question in view of the known pharmacologic properties of the drug.[18] In the opinion of the author, aminophyllin is capable of relieving the bronchospasm in both conditions and, therefore, its use in the mixed type of case sheds little light on the problem.

Digitalis is an excellent therapeutic agent in the treatment of a failing heart. It causes an increase in cardiac contraction with an initial rise in cardiac output, reduction of heart size, and a decline in the ventricular diastolic pressure. Thus a favorable response to digitalis might indicate a cardiac basis. In mitral stenosis, however, where the pulmonary congestion is a direct result of valvular obstruction, and in cases of high output failure, the drug is ineffective.

Mercuhydrin, on the other hand, is a drug that is extremely effective in all types of heart failure. Gold and his co-workers[19] have stressed its importance and demonstrated its usefulness not only in frank cases of congestive heart failure but also in cardiac asthma. Gelfand and Widlitz[20] employed mercuhydrin as an aid in detecting a cardiac factor complicating bronchial asthma. The dyspnea, cough, and pulmonary signs of bronchospasm resulting from true allergic bronchial asthma do not clear following an injection of mercuhydrin, whereas the same clinical picture when

due to cardiac asthma responds very favorably. Thus a positive response to mercuhydrin serves as a useful guide in differentiating cardiac from bronchial asthma. The increased usage of this drug would probably prevent many accidents in the treatment of bronchospasm of obscure etiology, and in cardiac asthma it would definitely prolong life.

From this discussion it is apparent that the differential diagnosis between cardiac and bronchial asthma is frequently a difficult task and taxes the ingenuity of even the keenest clinician. Many factors must be considered. The history (including family and past history), age of the patient, careful evaluation of cardiac function (including electrocardiographic and roentgen studies), skin tests, laboratory data (with particular attention to the circulation time), pulmonary-function studies, and the therapeutic response to various drugs including mercuhydrin are all important aids. Of these, however, the latter is of the greatest value. Its maximum usefulness exists in the elderly group, in whom a possible cardiac etiology must always be considered.

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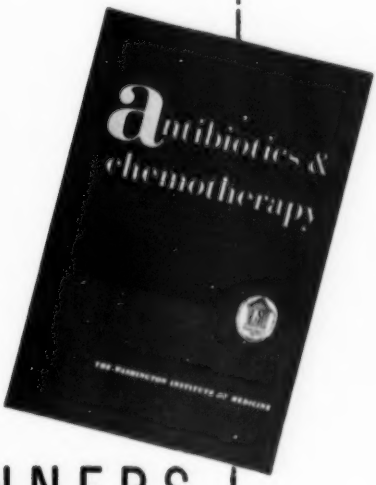

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16. Notes and Announcements

In fields which are developing as rapidly as are psychiatry and neurology, it is obviously impossible to abstract *all* the articles published—nor would that be desirable, since some of them are of very limited interest or ephemeral in character. The Editorial Board endeavors to select those which appear to make a substantial contribution to psychiatric and neurologic knowledge and which promise to be of some general interest to the readers of the REVIEW. Some articles, highly specialized in character, or concerning a subject already dealt with in an abstract, may be referred to by title only at the end of the respective sections.

A section entitled INTERNATIONAL RECORD OF PSYCHIATRY AND NEUROLOGY is included at the beginning of the journal. The Record Section consists of advanced clinical and experimental reports.

The Editorial Board at all times welcomes the suggestions and criticisms of the readers of the REVIEW.

WINFRED OVERHOLSER, M.D.
Editor-in-Chief

Quarterly Review of **PSYCHIATRY AND NEUROLOGY**

Incorporating the International Record of Psychiatry and Neurology

Psychiatric Perspectives in South America*

Winfred Overholser, M.D., Sc.D.

WASHINGTON, D. C.

In view of the recent extension of the activities of the American Psychiatric Association into the countries of the Caribbean area and the fact that South America is our close neighbor, the psychiatric activities of our colleagues in that vast continent are of immediate interest to us. During the period of World War II, under the "good neighbor policy" of President Roosevelt, a considerable number of psychiatrists, as well as of other physicians and members of other professions, visited this country for longer or shorter periods, so that many of us have had the pleasure of meeting some of our South American colleagues here.

Last December (1952), it was my pleasure and privilege to attend, by invitation and as representative of the American Psychiatric Association, the Ninth "*Jornada Nacional*," which was held in Santiago, Chile, to celebrate the centenary of the National Mental Hospital of that country, and to present to the group some facts as to the status of psychiatric education in the United States. These *Jornadas* have been held annually in various countries of South America under the auspices of the ten national psychiatric societies and have attracted a wide and representative attendance. In addition to my personal acquaintance, conversations, and correspondence with many South American psychiatrists, I have been aided in collecting these few notes by an article written in 1939 by Professors Delgado and Trelles of Lima, Peru, published in the Annales Médico-Psychologiques of Paris (Pt. 1, 97:567, no. 4, 1939), and a more recent compilation made by Doctor Miguel Nin of Cuba on the occasion of the First International Congress of Psychiatry in Paris in 1950 (Volume VI of the Proceedings, page 265).

In addition to the three small colonies of Great Britain, France, and the Netherlands, known as the Guianas, there are ten republics in South America, varying

*Remarks at International Symposium, American Psychiatric Association, Los Angeles, California, May 4, 1953.

greatly in size, in resources, in wealth, as well as in details of political organization. The language of these republics is Spanish, with the exception of Brazil, in which the language is Portuguese, a tongue which is closely related to Spanish and which is not different enough to interfere materially with communication. The professional people of South America, too, ordinarily speak two to three other languages beside their own, partly because that is the custom among educated men there, and partly because of the fact that for many years a considerable number of the textbooks used in the medical schools were printed in French, Italian, or German, and more recently in English.

Since South America was settled by colonists from the Iberian Peninsula it was natural that the ties intellectually and culturally should be with Europe and particularly with those European countries in which the Romance languages, French and Italian, are spoken. Thus we find that historically the influences which molded psychiatry in South America were largely those of the French school with an admixture of the German. In 1939 Doctors Delgado and Trelles said in their articles, referred to above: "We should note that the dominant influences are those of the French and German schools. The almost exclusive influence which the French clinicians exercised earlier has lost ground and today it shares its prestige with the German school. In certain aspects the Italian school also has exercised its influence." "Finally," they state, "we should note the influence of the American tendencies in everything concerning material details of psychiatric care, and above all mental hygiene." The article told also of the tendency to develop a spirit of solidarity among the Latin-Americans and what it terms a "continental consciousness," symbolized in the *Jornadas* such as the one recently held in Santiago.

The European war starting in 1939 changed the picture by almost entirely cutting communication between South America and the continent of Europe. At the same time, President Roosevelt emphasized hemispheric solidarity, developed the good neighbor policy, and encouraged closer contact between North and South America. With the increasing communication between the two continents it was only natural that the influence of American psychiatry should begin to be felt in the other half of the hemisphere. Since 1940, then, most of the psychiatric textbooks in use in the medical schools of South America have been North American. Some have been translated into Spanish, but many are used in the English edition. Many of those who are active in instruction in psychiatry have had much of their training in the States. One of the most conspicuous examples is Professor I. Matte Blanco of the University of Chile, who spent several years with Adolf Meyer at Johns Hopkins as well as a considerable period of time at the Maudsley in London. Dr. Alberto Seguin of Lima is, of course, widely known for his work in psychosomatic medicine, training for which he received in New York City. Baltazar Caravedo, Jr., had training with William Healy at the Judge Baker Guidance Centre in Boston, and Professor Alvarez of Paraguay spent a year in the United States. These are just samples of the trend toward North American relationships which are exhibited in the medical schools of South America.

In the field of medical education, Brazil is perhaps as advanced as any nation. The Rockefeller Foundation built an excellent medical school in São Paulo over 20

years ago, and the State is now building a two-hundred bed psychiatric clinic which will be used not only for teaching but for research. This work is under the charge of Dr. A. C. Pacheco e Silva, whose son likewise is a psychiatrist, trained at the Institute of Living in Hartford. In Santiago (Chile) a new psychiatric pavilion is being built, which will be utilized primarily for teaching under the direction of Dr. Matte Blanco.

In Ecuador the chair of psychiatry was established at Quito only in 1915, and as recently as 1938 in the other two medical schools of that country. Psychiatry is given in each of the fourth and fifth years of the medical school course. In Peru the work at Lima has been for many years under the direction of Dr. Honorio Delgado, one of the most distinguished of all the South American psychiatrists. Psychopathology is allowed 22 hours in one year, and in the other year about 25 hours are devoted to special psychiatry. In addition courses are given in medical psychology and in psychosomatic medicine. A large part of the instruction seems to be didactic.

An interesting point in connection with medical education in South America is that so far as can be learned all of the degree-granting institutions are under the control and operation of the State. In São Paulo there are two other medical schools beside the University of São Paulo, but neither of these is allowed to grant degrees; the students transfer at the end of their course over to the State University to obtain their degree. The graduate of a medical school is automatically, by the fact of his graduation, entitled to practice. There have been some indications in the public press that recently difficulties have been encountered by professors or candidates for faculty appointment in Argentina (where the universities are likewise operated by the State) who differ politically from the regime.

As for practice, it may be reported that in general the development of psychiatry is progressing very favorably. Each of the ten republics has at least one psychiatric society and in addition several more local ones such, for example, as the Society of Neuropsychiatry and Legal Medicine of Lima. Interest in the practice of psychoanalysis likewise is developing, particularly in Argentina and Chile. The work of Dr. Alberto Seguin in psychosomatic medicine in Lima has already been mentioned. It should also be recorded that clinics in child psychiatry have been developed both in Lima, under Dr. Baltazar Caravedo, Jr., and in Santiago, Chile, under Dr. Carlos Nassar. Electroshock and insulin therapy seem to be moderately popular, but interest in lobotomy does not appear to be especially widespread, although Dr. Mario Yahn, of São Paulo, has written some reports of his experience with this latter procedure.

As for the institutional care of the mentally ill, it must be said that the situation is, so to speak, somewhat spotty. There are several large areas of population in South America, such as the large cities of Rio, São Paulo, Lima, Santiago, and Buenos Aires, but vast parts of that continent are extremely sparsely settled and are at very considerable distances from centers of population. In Chile, for example, a country somewhat over 2,000 miles long, there is only one national mental hospital, that being located at Santiago, about the center of the country. Although it is intended ultimately to have a mental hospital in the north and one in the south,

the fact remains that at the moment it is extremely difficult for many patients to be sent to the hospital, or once sent, for their relatives to visit them. There are, for at least temporary care, a psychiatric service in the general hospital at Valparaiso and one at Concepcion, and a number of private mental hospitals are found near the centres of population in Chile and the other counties as well. Family care has been developed and was used at São Paulo as early as 1908. Also in Brazil and more recently in Chile there have been annexes of the mental hospitals to which they apply the term "The Open Door." These are, as the name implies, colonies with a minimum of supervision and control, where continued-treatment patients are able to work on farms. The ratio of beds to population, largely, perhaps as a result of the rural scattering of the population, is low compared with North American standards, being probably on the average substantially less than 200 per 100,000 of general population. Uruguay and Peru seem to have about the best ratios of approximately 110 per 100,000, while Chile, for example, has about one half of that.

Many of the psychiatrists in practice in South America are already Corresponding Members of the American Psychiatric Association, and they have all appeared to be enthusiastically ready for closer relations with their North American colleagues. There are, perhaps, as many as 16 psychiatric journals regularly appearing in South America, some of which exchange with our periodicals. There is every reason to think that the influence of North American psychiatrists and psychiatry will continue to grow in South America, and it is certainly to be hoped that more of our members will visit their colleagues to the South. They may be assured of a warm welcome, and will undoubtedly return with a deeper appreciation of the various significant activities in the psychiatric field which are going on in the other half of our hemisphere.

On the Basic Interconnection between Psychic Masochism and the Pseudomoral Connotation of Neurotic Symptoms

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NEW YORK, N.Y.

Psychic masochism has gradually achieved the unenviable status of "whipping boy" among all unconscious defense mechanisms. To begin with, its importance has been thoroughly neglected in psychiatric and psychoanalytic therapy. Moreover, the suggestion that psychic masochism be put in the center of that complicated web, the neurotic structure, met with a series of contradictory objections ranging from "it's old stuff" to "it's too complicated." The situation became so confused that the present writer has tried to clarify the issue (in *The Basic Neurosis*) by enumerating and discussing ten scientific and ten popular misconceptions, all twenty centering around psychic masochism.

The "old stuff" objection was based on a clear-cut misunderstanding: the *genetic* and the *clinical* pictures were confounded. It is true that Freud described the genetic picture, consisting of aggression turned inward because of guilt, secondarily leading to a libidinization of this guilt. This description was contained in Freud's *Collected Works;* it remained there, forgotten and unutilized, like some antiquated and unapplied laws that lie buried in our statute books. What was living reality can best be expressed in Freud's own words: "Another motive of 'opposite wish dreams' lies so near that one easily falls into the trap of overlooking it, as has happened to myself over a long period of time . . . the masochistic component." (*Gesammelte Schriften*, III, p. 30.)

The author's contribution to the problem consisted of working out the clinical picture in psychic masochism, and connecting it with the earliest level of development, the oral phase. The "mechanism of orality," embodying the final fate of psychic masochism, is made up of these successive steps:

a. Through their behavior, or the misuse of an external situation, neurotics unconsciously provoke disappointment and refusal, identifying the outer world with the "refusing" pre-Oedipal mother.
b. Not realizing that they themselves have brought about this disappointment, they become pseudo-aggressive, acting in righteous indignation and seemingly in self-defense.
c. They then consciously indulge in self-pity, unconsciously enjoying psychic masochism: "This can happen only to me."

The transition from the clinical to the genetic picture is accomplished because of the veto of inner conscience, which objects to the unconscious ego's "making pleasure out of displeasure."

The rejection of psychic masochism on the grounds that it is too complicated can be credited to inertia of the familiar type: "My learning days are over."

As the years have gone by, psychic masochism has achieved some stature—among patients. A grotesque state of affairs came into being: patients who had been unsuccessfully treated for years, in a therapy which excluded the masochistic sector of the personality, began to read up on the subject and bother their therapists with this problem.

Few adherents of dynamic psychiatry have so far taken serious cognizance of the painful fact that psychic masochism exists and is universal. These few now find their original oversight astonishing. In a recent discussion with one of the oldest and most astute of the old guard of Freud's pupils (he has been in practice for nearly fifty years), the author asked how such an oversight can be explained. The answer was laconic: "*The fourth narcissistic hurt.*" The colleague was referring to Freud's famous dictum that humanity has suffered three great narcissistic defeats: Copernicus proved that the earth is not the center of the universe; Darwin that man is not the unique crown of creation; Freud that man is not even master in his own house.

Psychic masochism does exist, and it plays a decisive rôle in every neurosis. The problem has been dealt with at length in this writer's books: *The Battle of the Conscience* (1948), *The Basic Neurosis* (1949), *Neurotic Counterfeit-sex* (1951), *The Superego* (1952). It is impossible to reproduce the contents of 1400 printed pages in a few sentences here.

Two newer misunderstandings stand out, however. To answer these: the existence of psychic masochism does not invalidate accepted rules of psychiatric-analytic procedure (it merely adds a new facet); adherents to the view that psychic masochism is of paramount importance do not advocate the simplification that the patient need only be told that "he unconsciously enjoys suffering."

As usual, things are slightly more complicated. First of all, psychic masochism cannot be explained without taking the structure of the inner conscience (super-ego) into consideration. This is so out of necessity, because psychic masochism is not a drive but an unconscious defense mechanism, created by the unconscious ego. The constant torture emanating from the super-ego is countered by shortchanging displeasure into pleasure. And the only pleasure one can derive from displeasure is to make out of that displeasure—a pleasure.

Secondly, psychic masochism cannot be explained without focussing attention on infantile megalomania. What is frequently overlooked is the long established fact that every frustration has two results: megalomania is offended, and a libidinous frustration added. Both results produce fury, and exactly this fury remains inexpressible for years in the infant, baby, and young child. The inner handling or mishandling of this fury determines the outcome quoad quantity of psychic masochism. Moreover, infantile megalomania is very specifically included in the psychic masochistic "solution" which is later arrived at; reduced to a caricature, the formula reads: "It is not the bad mother (or her successive representatives) who is punishing me; *I*, through my initial provocation, *made her* punish me."

Thirdly, there is a constant reformulation of oral-megalomaniacal material in the "language" of later developmental stages.

Fourthly, psychic masochism is not encountered without a series of inner alibis. Among these, some are already included in the previously quoted mechanism of orality. For example, the psychic masochist constantly operates on the assumption that he is the innocent victim of other people's meanness. Having repressed his own initial provocation—which started the eight-ball rolling—he fights with great energy (pseudo-aggression) for his rights.

Fifthly, nothing renders a psychic masochist more helpless than the unusual situation in which the alleged adversary does not allow himself to be provoked. The poor masochist is left like a fish out of water; attempting to recover, he increases the stake by increasing his provocation. The whole effect of therapy rests on a constant reduction of this technic to absurdity in the transference.

Sixthly, psychic masochists all work on the principle of the "pseudo-moral connotation of neurotic symptoms." This principle, first stated by the author in *The Psychiatric Quarterly* ("On a specific source of resistance in psychotherapy hitherto underestimated: The quasi-moral connotation of neurotic symptoms," 26:250–269, 1952), and later enlarged in *The Superego*, denotes:

Without exception, the secondary defense embedded within every symptom also contains a mocking irony directed against the internalized educators. Moral precepts actually communicated to the child during the educational process, and later also embodied in the ego ideal, are secondarily reproduced literally by the unconscious ego, where literal repetition—at the *wrong* time, in the *wrong* place, on the *wrong* occasion, out of context, and with *wrong* intention—does not reflect, but rather distorts, the meaning originally intended. The result is a *reductio ad absurdum* of the original meaning. This ironic technic of immobilizing the power of Daimonion (the accumulation of the child's rebounding aggression, amassed within the inner conscience) by speciously fulfilling the demands of the ego ideal (hence neutralizing the weapon of torture) corresponds to one of the few pseudo-aggressive retorts of the otherwise weak unconscious ego. The technic strengthens the unconscious ego's ability to create and maintain the spurious secondary defense. This pseudomoral connotation proves to be a powerful unconscious weapon of resistance. It is exactly the strength of this defense which has so far been undervalued in its universality. As examples, the following cases can be adduced:

An orally regressed woman remembered the following incident after hearing an explanation of this mechanism. Her father, a rigid educator, had specifically forbidden the children to pick any of the fruit from his prized apple orchard. When harvest time came, he discovered that the apples had been left on the trees, but this girl had been climbing the trees and nibbling the apples as they hung from their stems. The father's severe reprimand was countered with an impeccable argument. "You didn't say anything about eating. All you said was, 'Don't pick!' "

A young man with severe masochistic personality neurosis and inability to work, who also suffered from "psychogenic oral aspermia,"[9] persisted for a long time in his refusal to take a certain technical examination. "Take this idiotic examination!" his infuriated father would demand. "I am not thoroughly prepared yet," was the son's constant reply. The superficial layers of his examination-fear were easily explained. His father had tried to teach him the alphabet at the age of four; dissatisfied with the child's progress, the father constantly complained that he was not thorough enough in his studies. Two decades later, the son executed his (by then) full-fledged masochistic neurosis (also manifested in his wish to fail the examination) via pseudo-aggression: "Well, I'll give you thoroughness till you're blue in the face!" The fact that the

student damaged himself more than he did his father is another story . . . . Once more, blame for the lesser crime (pseudo-aggression) is accepted, once more the quasi-moral connotation of the secondary defense is obvious: "What's wrong with doing as father said, and being thorough?" Time, place and occasion are of course different, so that father's demand is reduced to absurdity—another characteristic quality of the pseudo-aggressive defense.

A girl with severe agoraphobia understood in analysis that her original wish had been voyeuristic; guilt had been shifted to the exhibitionistic defense, and the inner battle was fought on "foreign territory." All her secondary defenses (avoidance of the street, fear of entering the street, etc.) were fastened to the shift. The tenacity of her defense was bolstered by a series of educational commands which ostensibly encouraged exhibitionism. "Show your aunt your new dress," her mother had said once. And, "Why don't you play that new song you learned on the piano?" And, "Show us the little drawing that you made." In short, the unconscious ego here adduced, hypocritically, the exact statements made by educational authorities, and used them to prove that the defense (exhibitionism) was moral. Interestingly enough, the patient claimed that when the mother, fully dressed, bathes her naked child, she is issuing a double invitation to the child: to exhibit before the mother, and to abstain from looking at her (peeping).

This pseudomoral connotation has an astounding importance in maintaining the neurotic structure. As long as this inner irony is not debunked, and the specific and highly individualized features of the private moral code are not unearthed, one of the strongest pillars of neurosis simply remains untouched. This often leads to the erroneous assumption that the patient's unconscious is not giving in; actually, an oversight on the part of the therapist is to blame.

The question arises: what further connection, if any, exists between this pseudomoral connotation and psychic masochism? A connection does exist; this connection is basic and by no means tangential.

The amazing bellicosity of the psychic masochists is explained by the alibi to be presented to the super-ego: "I am not a seeker of displeasure, but an aggressive fighter for my rights!"

At the same time—and this is new—this fight for inner alibis also includes another sector consisting of the pseudomoral connotation: the precept dinned into the ears of the child: "Don't be a sissy, stand up for your rights and fight!" It is of course true that this precept was never meant to include provocatively induced sham battles. But this is precisely the basis of the pseudomoral connotation; to repeat the definition, precepts actually communicated to the child are mockingly distorted by being applied at the wrong time, in the wrong place, with wrong intention. The technic of "taking literally" reduces to absurdity the educational meaning originally intended.

Precisely this basic interconnection between psychic masochism and the pseudomoral connotation explains why it is not enough, in treatment, to repeat like a parrot that the patient takes "unconscious pleasure in self-damage." Exposing the neurotic to this *per se* correct interpretation is quite insufficient when, at the same time, the props provided by the pseudomoral connotation of the symptom itself remain standing. Only an attack on both sectors has a chance of destroying, or at least diminishing, the psychic masochistic structure.

If one asks why the pseudomoral prop is so important, the answer hinges on the pseudo-aggression included in it. Since the main reproach of inner conscience per-

*The case is described at length in *Neurotic Counterfeit-Sex*, Chapter III.

tains to indulgence in passive masochistic pleasure, the alibi of pseudo-aggression becomes a powerful counterargument of the weak unconscious ego. Result: neurosis is maintained. Thus, the pseudo-aggressive defense always includes the pseudomoral mockery of educational commands.

This deduction proves, by the way, the nonsensical element in the previously noted objection to the effect that "all the patient hears is that he is a psychic masochist." True enough, it is possible to schematize the interpretation of psychic masochism. But it is *not* possible to schematize the search for the hidden meaning in the *highly individualized* pseudomoral connotation. In any case, stressing the psychic masochistic substructure in neurosis is not likely to become a pons asinorum.

To adduce an example which combines the basic interconnection of both phenomena discussed here: A woman of means married a schizoid young man, a masochistic provocateur of the purest variety. His relationships in business consisted of senselessly making enemies in great quantity; the situation at home deteriorated to such an extent that the young matron could not bear to be touched by her husband. In spite of all that, she was sticking it out with a peculiar loyalty. The patient (analyzed by an experienced colleague) was shown her deep masochistic attachment. Nothing changed in her attitude. What was initially overlooked was an odd elaboration of a specific sector of her infantile conflict: her father, married to a psychotic woman, remained united with her, although even the patient understood as a child that "mother was more than peculiar." It turned out that the impossible husband of the daughter was a duplicate of the impossible mother. The young patient unconsciously identified with her father, repeating his masochistic martyrdom. The pseudomoral connotation read: "Should marriage not be maintained under any conditions? Father proved what he preached!" Behind this pseudomasculine identification, the whole unresolved, half-homosexual conflict with the pre-Oedipal mother lay hidden. The interpretation of the patient's psychic masochism was insufficient, as long as the pseudomoral prop was not removed.

ABSTRACTS

psychiatry

ALCOHOLISM AND DRUG ADDICTION

For Reference Only

73. *An Activity Program With Alcoholics.* JOAN M. DONIGER, Washington, D. C. Am. J. Occup. Therapy. 7:110–112 and 135, May-June, 1953.

BIOCHEMICAL, ENDOCRINOLOGIC AND METABOLIC ASPECTS

74. *Patterns of Biochemical Organizations Related to Morphology.* NATHAN S. KLINE, NANCY WERTHEIMER, CORA G. DYER, ANNA SCHENCKER, BETTY RUBIN, AND ROLAND SNIFFEN, Worcester, Mass. *109*:603–11, February 1953.

In an effort to develop the method of personality description capable of encompassing the findings of the various sciences, a series of preliminary experiments were carried out. Since such a conceptualization must be in terms of organization, patterns of response were selectively investigated. Form (somatotype) is probably a rough external representation of organization. Sixteen serological and biochemical indices were measured on three successive days on 35 female patients. On 15 male patients, five daily determinations were made on each of fifty indices. Significant linear correlations between somatotype and a large number of these indices (including albumen, globulin, blood sugar, etc.) were found. More discriminant nonlinear patterns were found in respect to other indices, such as sodium, potassium, uric acid, and 17-ketosteroids, in respect to both morphology and sex. Other work is reported in which the same types of patterns were found with blood pressure and pulse rate.

By crosscorrelations of the various indices, individuals were shown to have a typical response pattern relative to the rest of the group, which is apparently even more reliable than patterning related to morphology. The implications of these results for psychiatry and medical science in general were discussed. 17 references, 10 figures, 3 tables.—*Author's abstract.*

CLINICAL PSYCHIATRY

75. *Deterioration in Dementia Paralytica.* V. A. KRAL AND HERBER DORKEN, JR., Montreal, Quebec. Am. J. Psychiat. *109*:684–92, March 1953.

A comparative serologic and psychologic investigation of 52 institutionalized cases of dementia paralytica under 60 years of age was made. The Rorschach and

Wechsler-Bellevue Intelligence Scales were administered to 26 of the subjects, psychometric data being unobtainable from the others.

A sex difference among the cases with negative (post-treatment) spinal fluid in the nature of more pronounced dementia among the men was noted. The data indicate that deterioration may continue despite a negative spinal fluid spectrum. The activity of the disease process was found to have an extensive influence on the personality and intelligence of these subjects, the tests demonstrating a more marked impairment among the cases whose spinal fluid was negative. These findings imply that at least two factors have to be considered in the pathogenesis of general paresis. It is suggested that one is the inflammatory component, which is reversible with treatment, and the other a vascular factor which is not easily influenced by therapy and which may be progressive despite the fact that treatment resulted in a negative spinal fluid spectrum. Neither the nature of the prepsychotic adjustment nor a history of alcoholism showed any significant difference between the sub-groups. However, more extensive neurologic signs were present in the group of deteriorated patients with negative in comparison to those with a positive spinal fluid. The psychologic deficit found in dementia paralytica appears to differ from that of senile dementia. 27 references. 4 tables. *Author's abstract.*

76. *Premenstrual Tension: EEG Hormonal and Psychiatric Evaluation.* WANDA M. LAMB, GEORGE A. ULETT, WM. H. MASTERS, AND DONALD W. ROBINSON, St. Louis, Mo. Am. J. Psych. *109*:340–48, May 1953.

The occurrence of premenstrual tension in such a large segment of the female population has not been adequately explained. Because of the prominence of psychiatric symptomatology in this disorder, it indicated a need for investigating the possibility of a correlation between these symptoms and some specific personality configuration. It was felt, also, that by simultaneous physiologic and psychiatric observations on a group of subjects with premenstrual tension and on a group of controls, other correlations might become evident. An electroencephalographic investigation was included to determine whether or not behavioral manifestations might reflect directly alterations in the cerebral neurophysiology so measured.

A questionnaire study was made of 127 student nurses, covering menstrual history, pelvic disease, and family history of menstrual symptoms. From this group, 5 subjects with premenstrual tension and 5 controls were studied in detail throughout two complete menstrual cycles. Pelvic examination was done on each subject. Pituitary, thyroid, and ovarian functions were investigated by means of gonadotropic titers, basal metabolic rates, and vaginal smears. Eight one hour interviews were held with each subject, scheduled at 24 hours postbleeding, the time of ovulation, the premenstrual period, and the first day of bleeding. This afforded opportunity fer direct observation of changes in the subject's behavior during the various phases of the menstrual cycle and for assessment of the general personality configuration of each subject. Electroencephalographies, with photic

stimulation, were recorded in the 24 hour period postbleeding, at the time of ovulation, and in the three day period prebleeding.

This study reveals no evidence that would substantiate a theory of psychogenic etiology for premenstrual tension. No *sine qua non* conditions for the occurrence of premenstrual tension were found. However, there appeared to be some definable differences in behavior other than the premenstrual manifestations, differentiating the two groups of subjects. The subjects with premenstrual tension showed more marked emotional lability throughout their cycles and, in general, were less assertive individuals. Electroencephalographic investigation gave no indication that the behavioral manifestations of premenstrual tension reflect directly alterations in the cerebral neurophysiology so measured. There was a decrease in alpha activity in the control group in the immediate premenstrual period, contrary to what one would expect on the basis of the known effect of "tension" on alpha activity in the EEG. Endocrine activity was within normal limits in all subjects, with no demonstrable distinction between subjects with premenstrual tension and controls, which would tend to contradict the concept that estrogen-progesterone imbalance is necessarily associated with premenstrual tension. Using weight change as a rough criterion of water metabolism, water retention appeared to occur more often among the controls than among subjects with premenstrual tension. 11 references. 1 figure. 5 tables. *Author's abstract.*

77. *Some Present-Day Aspects of Military Neuropsychiatry.* JOHN J. MARREN, Tacoma, Wash. Northwest Med. 52:107–11, February 1953.

A large fund of military neuropsychiatric knowledge, accumulated during World War I, had largely been forgotten or ignored in military planning by the time World War II appeared. The impact of Pearl Harbor found the nation without the manpower and specific plans to meet the tremendous and immediate demand for psychiatric service that mass mobilization imposed upon it. The North African invasion focused attention upon deficiences inherent in the management of the neuropsychiatric combat casualty as practiced in the early years of World War II. In North Africa, with neuropsychiatric facilities sometimes a hundred miles from the front, only 5 per cent of neuropsychiatric battle casualties were returned to combat. With reinstatement of the division psychiatrist in the combat division's table of organization and assigning each field army a psychiatric consultant, at the time of the Normandy invasion up to 65 per cent of combat neuropsychiatric casualties were returned to duty in the combat area. Lessons learned in the cauldron of World War II have been set forth in official military directives to act as a guide and plan for the management of neuropsychiatric battle casualties in future conflicts. These directives have been employed in organizing the methods of screening and treating neuropsychiatric casualties in Korea with some forward neuropsychiatric hospital installations reporting 65–70 per cent of psychogenic combat casualties being returned to duty, with 45 per cent being assigned to full duty. 19 references.

PSYCHIATRY AND GENERAL MEDICINE

78. *A General Hypothesis of Psychosomatic Disorder.* J. O. WISDOM. Brit. J. M. Psychol. *26*:15–29, March 1953.

The work of Alexander, Deutsch, and Selye is reviewed. The most general problem is posed of why one person develops a psychosomatic and another a purely psychologic disorder. A theory is then put forward to explain this, in the form of explicit hypotheses, for which empirical tests are suggested.

A sharp distinction is drawn between "projective" images, such as visual images, and tactile and kinaesthetic sensations. It is held that frightening images approach the person who has them, but do not arrive, and are kept at a safe distance, to prevent corresponding sensations from arising. Anything tending to arouse an unwelcome sensation could be mastered by substituting a projective image for it. This leads to Hypothesis V: A purely psychological disorder is one in which the imagination conducts basic conflicts in terms of projective images; a psychosomatic disorder is one in which the imagination conducts basic conflicts in terms of tactile or kinaesthetic sensations. Case reports bearing on this are cited.

An application to peptic ulcer is considered: if a person's greed conflicts are conducted in projective imagery, this would not, according to the hypothesis, affect the digestive system; but if conducted in terms of tactile or kinaesthetic sensations it would do so, and thus cause the hypersecretion of acid.

Some modifying hypotheses are mentioned and another paper of the author's cited to provide a model of mind-body interaction.

Defence mechanisms are considered to explain why one person may succeed, and another fail, in conducting their basic conflicts in projective imagery, thus avoiding a psychosomatic disorder; when the defence mechanisms fail, the conflicts move to the domain of sensation and produce psychosomatic disorder.

Several kinds of test are mentioned: these depend on the neurologic, hypnotic, and psychoanalytic consequences that follow from the theory. 50 references.—*Author's abstract.*

For Reference Only

79. *Psychiatric Factors In Dermatologic Disorders.* ALBERT J. SILVERMAN, Denver, Colo. Am. J. M. Sci. *226*:104–109, July 1953.

PSYCHOPATHOLOGY

80. *The Role of Anxiety in the Physician-Patient Relationship.* SPENCER F. BROWN, Minneapolis, Minn. Journal-Lancet *73*:47–50, February 1953.

The patient's anxiety—referring here to uneasiness caused by circumstances related to physical illness which threaten the patient—is one of the most important factors in the physician-patient relationship. It serves, first, to drive the patient to seek medical attention, either because his physical symptoms arouse anxiety, or

because worry over other matters makes the additional anxiety created by the illness unbearable. Anxiety, if too great, may also prevent the patient's seeking medical aid for fear of an unpleasant examination or a frightening diagnosis. Often a patient's choice of physician is determined largely by the doctor's ability to relieve his anxiety, although such relief may be provided in widely varied ways for different patients. Anxiety may also determine the extent to which the patient follows the prescribed treatment; for when his fears subside so, often, does his motivation to follow his doctor's orders. In the case of pediatric patients, the foregoing applies particularly to the parents, although the patient's anxiety, especially concerning the examination, should also be considered.

While anxiety is not the only important factor in the physician-patient relationship, recognition of its rôle in the patient's attitudes and behavior will help most physicians to help their patients more effectively. 3 references.

TREATMENT

a. general psychiatric therapy

81. *Methods of Treatment of Delirium Tremens.* JACKSON A. SMITH, Houston, Texas. J. A. M. A. *152*:384-87, May 30, 1953.

Delirium tremens is a toxic state occurring after a prolonged alcoholic bout and characterized by an incipient stage of apprehension, insomnia, and tremor ("the shakes") followed by a stage of active delirium in which the patient is confused, disoriented, and agitated ("the horrors"). Postulated etiologic factors in addition to the excessive alcoholic intake include abstinence, a "toxin," cerebral edema, avitaminosis, and exhaustion of the adrenal cortex.

In the past, the following treatment regimens have been recommended: spinal drainage, dehydration, hydration, digitalis, vitamins, adrenocortical extract, and adrenocorticotropic hormone. The consistent feature in the treatment of delirium tremens appears to be a decrease of about 50 per cent in morbidity and mortality whenever some new treatment regimen is tried. It is presently advocated that physiologic normalcy be re-established by correcting the evident systemic dehydration, malnutrition, vitamin deficiency, and electrolyte imbalance. Sedation with paraldehyde or chloral hydrate and a long-acting barbiturate, with physical restraint only to prevent the patient doing himself harm is recommended. 11 references.—*Author's abstract.*

b. drug therapies

82. *Sensitivity in Insulin Coma Therapy.* ALBERT E. SCHEFLEN AND ELLIOT R. REINER, Worcester, Mass. J. Clin. & Exper. Psychopath. *13*:225-36, December 1952.

The subjects were 100 schizophrenic patients successively treated with insulin coma therapy with fifty comas constituting a course. Excluded were those with

definitive physical disease, significant untoward reactions, insufficient clinical data, or uncertain improvement. There remained 37 women and 30 men. The group included the 24 male patients previously studied. An analysis of psychiatric factors is published elsewhere, and the method of assessing improvement is described in a companion study. Supervising the insulin unit were several physicians, not the authors, who differed in their methods. This resulted in diverse, sometimes unusual methods of dose administration, which precluded certain statistical assessments but gave an opportunity to contrast and study the effect of methodology. Insulin was not given intravenously and adjunctive medications were avoided. Dose, depth of coma, time intervals, vital signs and other clinical factors were measured and analyzed as previously described. To measure sensitivity to insulin the authors used: (1) the insulin dose effecting coma; (2) the frequency of treatments unsuccessful in producing coma, expressed as a coma: treatment ratio; and (3) the depth of coma or the frequency of third stage coma. As will be seen these factors affected one another: measures (1) and (2) correlated positively; (1) and (3) negatively.

It was found that the dose level which a patient seemed to require for comas depended a great deal upon the dose selected by the clinician. Early in treatment it seemed that physiologic resistances to coma were present and that these had to be overcome by successive daily insulin injections rather than large doses.

There was some evidence that there are two levels of sensitivity: lower level used below 250 units, and an upper level, above 400 units. It seemed difficult to produce coma between 250 and 400 units.

There were a number of statistically valid relationships between the vital signs and the insulin dose employed. At above 350 units, the dose required for coma correlated positively with the blood pressure, basal and during coma. Surprisingly enough, doses below 250 units were significantly more likely to produce a deep coma than were higher ones, and coma began more quickly with the lower doses. Evidence was reviewed to show that comas may be produced by reducing doses to the lower level of sensitivity rather than increasing them. With marked sensitivity to insulin, certain clinical characteristics are seen, which are suggestive of parasympathetic predominance and/or adrenocortical deficiency.

Certain clinical factors which affect insulin sensitivity were statistically analyzed. Most essential were (1) method of selecting dose, (2) improvement in psychiatric state, and (3) hirsutism in women. Sensitivity on individual days was affected by (1) cooperativeness to treatment, (2) electroshock convulsions, (3) low environmental temperatures, (4) stage of treatment course and (4) day of the treatment week. These observations were related to the General Adaptation Syndrome. Biochemical studies by other authors indicated that high insulin requirements are related to high blood adrenalin levels. It was hypothecated that use of doses of insulin in general above 250 units may increase resistance to insulin by stimulating an epinephrine-like defense and that this explains many of the clinical aspects of insulin therapy and permits an improved rationale of therapy. 20 references. 2 tables. — *Author's abstract.*

83. *Narcosynthesis Effects of Sodium Amytal Methedrine and L. S. D-25.* SOLOMON KATZENELBOGEN AND AI DING FANG. Dis. Nerv. System *14*:85-88, March 1953.

Sodium amytal, methedrine, and L. S. D-25 were studied in 20 patients under similar conditions.

Methedrine was administered intravenously in amounts from 5 to 20 mg.; 10 to 15 mg. seemed to be most effective. The drug was administered two or three times at intervals of three to five days or longer. In order to facilitate the intravenous administration of the drug in appropriate dosage, the authors diluted the 1 cc. ampule containing 20 mg. of the drug with 3 cc. of the distilled sterilized water. The physiologic and personality reactions were noted for one hour following the injection.

Sodium amytal was given intravenously in amounts from .3 to .5 Gm. to each patient only once. The patients' reactions were observed during and one hour after the injection.

L. S. D-25 was given by mouth. The content of the ampule (0.1 mg. of the active substance) was diluted with 9 cc. of distilled water; this *oral solution* should be made and stored in a dark bottle. It should not be used beyond the third day after preparation. The dosage varied from 1 to 5 cc. of the *oral solution;* 2.5 to 4.5 cc. appeared to be most effective. The patients' reactions were noted within two or three hours after the administration of the drug.

The physiologic reactions of the authors' patients to methedrine and L. S. D-25 were preponderantly sympatheticotonic, and to sodium amytal parasympathetico-tonic. Because of the longer duration of the effects of methedrine and L. S. D-25 than of sodium amytal, the patients had more time for ventilating their emotions and for verbal production with these two drugs than with sodium amytal.

Methedrine and L. S. D-25 have raised the blood pressure in the patients, whereas sodium amytal had rather hypertensive effects; the latter drug is therefore preferable in patients with high blood pressure. 3 tables.—*Author's abstract.*

c. psychotherapy

84. *The Nature of Psychotherapy.* ALFRED BRONNER, Passaic, N. J. J. M. Soc. New Jersey *50*:68-71, February 1953.

Psychotherapy must be a fundamentally new experience to the patient. Its newness, uniqueness, and therapeutic value stem from the emotional insight obtained. The emotional charges released make psychotherapy a living experience which is difficult to describe.

The concept of anxiety, i.e., "the fear from within" is the key to our understanding of psychoneurosis and also therapy. In the adult, anxiety occurs in response to the patient's own aggression and/or sexual drives, the nature of which is not clear to the patient. To the trained observer anxiety represents the once real or imaginary fear of punishment, which the authority figures (i.e., the parents) could elicit

because of transgression of their prohibitions. The conscience of each individual represents an incorporated condensation of such prohibitions. Since anxiety is only felt as a serious discomfort, defensive maneuvers are spontaneously employed to lessen the discomfort. The symptoms of neurosis distract attention from the anxiety-producing impulse, although they often contain concealed evidence of such impulses. In therapy it is impossible to reason the symptoms away. They will disappear when their protective function is no longer needed.

Concealed or open hostility to the therapist will appear without fail during treatment. It appears in spite of the therapist's friendly neutrality. Earlier aggressive drives are transferred to him as he begins to assume the quality of an authority figure to the patient. In due time such transference of earlier attitudes can be interpreted and explained. Its "irrational" quality becomes clear and old anxieties fade away in preference of a more realistic relationship to the environment. Since such a process seeks out anxiety-filled memories and ideas, a "resistance" appears in treatment. This resistance is not deliberate but a spontaneous phenomenon. It can take many forms, such as being late or forgetting an appointment, having nothing to say or talking about irrelevant matters. A lengthy discussion of symptoms or pseudoscientific arguments between therapist and patient also serve the forces of resistance which have to be recognized and brought to the patient's attention.

Many factors influence the course of therapy. The personality of the therapist must be right for the patient in addition to the therapist's ability. The attitudes of the patient's close relatives are of great importance. Very often parents, wives, and husbands have preconceived ideas as to what the psychotherapy should do. They often disapprove, and even interfere when the patient begins to show signs of independence and self-reliance.

The physician referring the patient for psychotherapy should receive a diagnostic evaluation of the patient. The specific problems of the patient should not be divulged since absolute confidence in the psychiatrist's secrecy are the basis for treatment. Psychoneurosis presents a chronic illness and treatment of an uncovering type as described here is lengthy and costly. The success of treatment depends on the patient's ability to deal with past and present conflicts. Some patients are so inflexible that they feel threatened by any change. Yet, as in clinical medicine, a seemingly poor risk in therapy will sometimes show an amazing response.—*Author's abstract.*

d. the "shock" therapies

85. *The Use of the Electronarcosis Instrument for Several Types of Treatment.* LESTER L. BOWLES. J. of Clin. & Exp. Psychopath. *14*:78-83, June 1953.

Methods are described for the use of the electronarcosis instrument in giving the following four types of electric treatments: (1) combined convulsive and nonconvulsive, "Reiter" type; (2) combined, with succinyl choline dichloride; (3) short convulsive, "brief stimulus therapy" type; (4) nonconvulsive stimulation. Indications are given for the choice of type of treatment.

Opinions are expressed that the results obtained with the use of only the one instrument are comparable with those obtained with the several other instruments now in common use; also, that there are important differences in the effects of the different types of treatment as they are being used for various psychoneurotic disorders. It is hoped that increasingly safe, appropriate, and therapeutically satisfactory technics may emerge as methods are further modified in the light of increasing clinical experience. 8 references.—*Author's abstract.*

86. *The Treatment of Tuberculous Patients With Electroshock Therapy.* J. H. MC CLELLAN AND ABRAHAM SCHWARTZ, Los Angeles, Calif. Am. J. Psych. *109*:899–905, June 1953.

Since 1949, the authors have treated 23 patients in various stages of tuberculosis (mostly far advanced), and the improvement in their psychiatric symptoms has been generally gratifying. There have been no deleterious effects insofar as the tuberculosis was concerned, even after administration, in some instances, of prolonged shock therapy; on the contrary, there has been universal improvement in the pulmonary tuberculosis, with the exception of one patient.

From the authors' clinical experience with patients suffering from severe mental illness, aggravating and aggravated by advanced stages of pulmonary tuberculosis, they have no doubt about the value of electroshock therapy and its safety, in the treatment of such patients. Their results indicate that, when patients are so psychotic that they cannot cooperate in treatment for their tuberculosis, electroshock therapy may improve their mental status to the extent that they will accept treatment. The authors think that some of these patients might have been successful in their suicidal attempts, or have died as a result of the tuberculosis, had it not been for the use of electroshock therapy. Moreover, there appears to be a uniformly specific improvement in the pulmonary tuberculosis following ECT regardless of the stage of advancement when the treatment is started. This may be a secondary effect of electroshock therapy.

Some sanitariums allow patients to have passes for home visits. Activities remain uncontrolled during the entire period they are away from the hospital. We believe this may be more detrimental to their illness than the alleged dangers of electroshock. The authors' service has been visited by psychiatrists and tuberculosis specialists, who wanted to evaluate the results. The visitors expressed surprise at the favorable results obtained with the treatment the authors outlined. 2 references. 8 figures. 1 table.—*Author's abstract.*

87. *Hazards of Lobotomy.* WALTER FREEMAN, Washington, D. C. J. A. M. A. *152*:487–91, June 6, 1953.

Results in 2,000 lobotomy operations have been studied in regard to comparison of the standard prefrontal method and the transorbital method, particularly from the standpoint of the dangers of the two methods. Prefrontal lobotomy carries twice the risk of death from operation, 3.6 per cent as against 1.7 per cent. Mis-

placed incisions in the former and uncontrollable hemorrhage in the latter are the chief causes of death. Nonoperative fatalities occurring months to years after operation show a preponderance of cardiovascular deaths in prefrontal lobotomy and deaths from malignant disease in transorbital lobotomy. The latter finding indicates the use of transorbital lobotomy in the relief of terminal pain syndromes in carcinoma for which prefrontal lobotomy is needlessly drastic.

Physical complications such as obesity, hemorrhage, paralysis, and convulsions are shown to be ten or more times as common after prefrontal lobotomy as after transorbital lobotomy. While the convulsions can be brought under control in a fair percentage of cases, nevertheless, the trauma to the cortex in prefrontal lobotomy is an important predisposing cause. Probably the most feared result of lobotomy, namely the "frontal lobe syndrome," with its indolence, tactlessness, and lack of responsibility was found in 9.3 per cent of the prefrontal cases and only 0.5 per cent of the transorbital cases.

The final hazard in connection with lobotomy is the hazard of delay, of not performing the operation. It is shown on the basis of a thousand patients that two thirds can be restored to effective social existence if operation is performed in the first six months. The percentage falls to 50 per cent in the second six months and 36 per cent in the second year. Ten per cent of patients can still be restored to useful activity after hospitalization of seven years or more. Chronic mental disorder is a serious handicap to social readjustment in the patient who has undergone lobotomy. 9 references. 4 tables. —*Author's abstract.*

88. *A Comparative Study of Flaxedil and Syncurine Combined with Pentothal Anesthesia in Modifying Electroconvulsive Therapy.* WILLIAM L. HOLT, JR., Albany, N. Y., DONALD NISWANDER, DEWEY K. ZIEGLER, AND RICHARD TURK, Boston, Mass. Am. J. Psychiat. *109*:749–756, April 1953.

Twenty-one patients, 15 female and 6 male, ranging in age from 19 to 76, were given electroconvulsive therapy modified by the use of pentothal anesthesia and syncurine and flaxedil, the latter two drugs being used alternately. Skeletal musculature weakened because of the presence of heart disease, arteriohypertension, recent fracture, or unhealed laceration. Sufficient muscle weakening was obtained to prevent perceptible muscular hypertonus during the seizure or elevation in blood lactic acid. Blood pressure and pulse recordings were taken with the patient supine before the administration of any drug. Atropine sulphate was administered intravenously together with the pentothal, 0.9 mg. being given to block the vagus. The amount of flaxedil used varied between 80 and 120 mg. Syncurine was given in the amounts of 5 to 6 mg. Blood pressure and pulse were again determined immediately after the injection and three minutes later, immediately before the electric shock stimulus was given. In the experiments were flaxedil, the drug being tested, 2 mg. of prostigmine together with 0.6 mg. atropine sulphate given intramuscularly just before the electric stimulus. As soon as the seizure was ended, blood pressure and pulse readings were immediately taken.

In a majority of patients, there was less than 10 mm. change in blood pressure immediately following the injection of flaxedil and pentothal with atropine. In 5 patients a fall in blood pressure of more than 10 mm. occurred, the greatest fall being 60 mm. in a markedly hypertensive patient. Pulse rates rose an average of 20 beats. Immediately after the convulsion, blood pressure rose 50 mm. systolic but returned to pretreatment level within 15 minutes. Minor irregularities and change in rate occurred but were not consistent. Results with syncurine were essentially the same but the recovery period was more prolonged. The time of oxygen administration required after the seizure was cut in half by the use of flaxedil, as compared to the syncurine-treated cases. Respiratory obstruction was occasionally encountered when syncurine was used on some 97 patients and was not encountered in a group of 111 cases treated with flaxedil.

One patient suffering with angina suffered a myocardial infarction in the course of flaxedil-modified electroconvulsive therapy. This 72 year old woman made a good recovery as her infarct did not occur until the sixth treatment. Complete skeletal muscle paralysis does not prevent cardiovascular changes of central origin. Adequate pressure bag oxygenation throughout the period of skeletal muscle paralysis is essential. Flaxedil has the advantage of requiring less time for treatment. 3 references. 1 figure. 1 table. —*Author's abstract.*

neurology

CLINICAL NEUROLOGY

89. *Tic Douloureux of the Chorda Tympani.* SAMUEL ROSEN, New York, N. Y. Arch. Neurol. & Psychiat. *69*:375–78, March 1953.

A new method to determine differentially whether the seventh or ninth nerve is responsible for the ticlike pain in the ear is described. This consists of raising the ear drum out of its sulcus, under local anesthesia, and folding it upward upon itself thus exposing the chorda tympani and Jacobson's nerve. Electric stimulation of each separately evokes the nerve which gives the typical pain of which the patient complains. In 2 cases reported, the differential was made in this way, which is much simpler than the intracranial route. The condition was called tic douloureux of the chorda tympani nerve. 7 references. 1 figure. —*Author's abstract.*

90. *Sensory and Motor Loss After Non-Neural Injuries.* MICHAEL KELLY, Melbourne, Australia. Neurology *3*:327, May 1953.

Forty-three cases of motor and sensory loss followed damage to somatic tissue, which could not have injured any nerve trunks. The skin was punctured in only

15 cases: the injuries were mostly mild, though there were two severe sprains, two lacerated wounds, and three fractures of long bones. In 28 cases, the hand of the upper limb was injured; the paralysis usually came soon after the injury (though occasionally it has been delayed for months or even years).

Sensory or motor paresis, which may be complete or incomplete, varies from case to case, but sensory effects are more common than motor and spread more widely. The loss may be limited to a nerve field: more commonly it involves portions of the fields of two or more nerves. Localized and transient effects are common; spread to other limbs is uncommon and more likely to be reported in the literature. When the effect develops in another part of the body, it has been called reflex paralysis.

In the severe cases a painful disability may persist for years, and hysteria or malingering may be erroneously diagnosed. Operations to relieve supposed pressure on nerves are unsuccessful, and section of nerves intensifies the spread.

Ascending neuritis is not due to infection, but to chromatolysis of neuronal bodies in response to damage to the fine nerve-fibrils, which ramify in all somatic tissues. Though chromatolysis is usually inversely proportional to the distance of the lesion from the cell, occasionally an intense reaction is set up by minor damage at a great distance from the cell. The neuronal disturbance is transmitted through the synapses and spreads beyond the cells originally involved. 71 references. 1 figure. 1 table.—*Author's abstract.*

91. *Technique and Value of Myelography.* FRANK L. SHIPP, Boston, Mass. J. A. M. A. *151*:185-88, Jan. 17, 1953.

Since 1938, myelography has been performed on more than 3,000 patients by the orthopedic and neurosurgical services of the Lahey Clinic. Various contrast media have been employed, pantopaque being used exclusively since 1946 in over 1,300 instances, with no significant ill-effects attributable to the agent itself.

Myelography is employed routinely: (1) to confirm or to exclude the presence of an intraspinal lesion when clinical methods, including adequate roentgenograms, have failed to establish an unequivocal diagnosis; (2) to differentiate intervertebral disk protrusions from spinal cord tumors, to disclose multiple lesions, if present, and to localize any lesions thus found; (3) to investigate persistent or recurrent symptoms referred to the spine, in patients who have undergone previous surgery; (4) to exclude tumors or similar lesions in patients with a presumptive diagnosis of degenerative disease of the spinal cord; and (5) to exclude intraspinal disease in patients about to undergo a spine fusion, with or without laminectomy, particularly in cases of congenital bony anomaly.

Of patients requiring exploration of the lumbar spine for low back pain, 4.3 per cent have been found to suffer from tumors of the cauda equina. In cases of disk protrusion, approximately 14 per cent have involved more than one segmental level. Disk protrusions have seldom been found in combination with spondylolysis or spondylolisthesis.

The procedure is not recommended in the case of an obvious malingerer, except to exclude intraspinal disease or injury, nor in the case of a patient who is emotionally unstable or who is otherwise psychologically ill-adapted to any surgical procedure. 8 references.—*Author's abstract.*

ANATOMY AND PHYSIOLOGY OF THE NERVOUS SYSTEM

92. *Some Mechanisms of Tactile Localization Revealed by a Study of Leucotomized Patients.* ALICK ELITHORN, MALCOLM F. PIERCY, AND MARGARET A. CROSSKEY, London, England. J. Neurol., Neurosurg. & Psychiat. *15*:272–82, November 1952.

Tactile localization on the fingers has been studied pre- and postoperatively in patients undergoing prefrontal leucotomy. Although the frequency of gross errors was increased postoperatively, similar errors were made before operation, and it was concluded that the operation impaired an imperfect skill in an essentially nonspecific manner. The incidence of errors and the direction in which stimuli were erroneously referred were found to depend on the site stimulated. Thus the distribution of errors resulting from the subject's indicating the wrong finger (finger errors) was different from the distribution of errors resulting from the subject's indicating the wrong side of a finger (side errors). This suggests that the subject decides separately which finger and which side of a finger is stimulated. Further, the direction of referral of finger errors is positively related to the side of the finger stimulated, and the direction of referral of side errors is similarly related to the side of the hand (ulnar or radial) stimulated. This result has been interpreted as a confusion on the part of the subject between two standards of reference or "concepts," the side of the finger stimulated, and the side of the hand stimulated.

These observations are consistent with the hypothesis that normal tactile localization in man occurs through the intermediary of certain dimensions of orientation or concepts. The revelance of these observations to theories of postural orientation and orientation in external space is indicated. 7 references. 2 figures. 5 tables.—*Author's abstract.*

For Reference Only

93. *The Frontal Lobes.* FRANK R. ERVIN, New Orleans, La. Dis. Nerv. System *14*:73–83, March 1953. 100 references.

CEREBROSPINAL FLUID

94. *Observations on the Effect of Induced Hyperglycemia on the Glucose Content of the Cerebrospinal Fluid in Patients with Tuberculous Meningitis.* JOSE E. SIFONTES, D. BROOKE WILLIAMS, EDITH M. LINCOLN, AND HELEN CLEMONS. Am. Rev. Tuberc. *67*:732–754, June 1953.

A test was devised in an attempt to facilitate the early diagnosis of block in tuberculous meningitis and to clarify some of the abnormalities that occur in the

cerebrospinal fluid constituents of patients with tuberculous meningitis. Glucose was selected as the best substance; it was administered by the intravenous route in a 20 per cent solution in a dose of 1 Gm. per Kg. of body weight. Samples of 0.5 ml. of cerebrospinal fluid were withdrawn from the lumbar, cisternal, and whenever possible, ventricular region every 15 minutes for two hours after the injection of glucose.

Five children without meningitis and 6 children with healed tuberculous meningitis and no hydrocephalus, as demonstrated by pneumoencephalogram, showed similar curves, characterized by an increase in the glucose concentration of the lumbar and cisternal fluid of 30 to 60 mg. per 100 ml. above initial values. The maximum increase occurred between 45 and 120 minutes after the injection of glucose. The cisternal values were always slightly higher than the lumbar values.

Abnormal curves were obtained in children with active tuberculous meningitis and in children with hydrocephalus resulting from tuberculous meningitis. Abnormal curves are reported in 15 patients.

The main abnormalities consisted of: (1.) Decreased permeability to the passage of glucose during the acute phase in several but not in all children. (2.) Increased permeability in the lumbar region so that the lumbar curve rose above the cisternal in patients under treatment with intrathecal streptomycin or in patients with spinal block due to tuberculous meningitis. (3.) Flat ventricular curves in patients with hydrocephalus. The lumbar and cisternal curves were flat also in patients with healed tuberculous meningitis and residual hydrocephalus. In other patients with hydrocephalus elevations of the cisternal and lumbar curves were noted with the presence of spinal block or administration of streptomycin into the lumbar subarachnoid space.

With improvement in the tuberculous meningitis the abnormalities of the glucose curves disappeared. These findings suggest that marked alterations in the permeability of the meninges for glucose occur during the course of tuberculous meningitis; under abnormal conditions glucose can pass from the blood into the cerebrospinal fluid locally into any portion of the subarachnoid space; and that these changes may account for the low glucose values obtained in the permeability for glucose in the lumbar region observed in patients with spinal block and may facilitate early diagnosis of spinal block; however, interpretations of the curves should be tempered by knowledge of the effects of intrathecal streptomycin and the presence of hydrocephalus. 11 references. 16 figures.—*Author's abstract.*

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

95. *Seizures and Psychopathology in Multiple Sclerosis. An Electroencephalographic Study. Discussion of Pathogenesis.* VICTOR FUGLSANG-FREDERIKSEN AND PAUL THYGESEN, Copenhagen, Denmark. Acta Psychiat. et Neurol. *27*: 17–41, 1952.

A total of 74 patients with multiple sclerosis were followed up for an average period of nine months. Continuous clinical neurologic examinations were carried

out about every three weeks, and EEGs were obtained at average intervals of two and a half to three months (a total of 203 tracings).

In a previous communication the writers reported the results of a comparison of the clinical course and the EEG findings.

In the course of the observation period, 8 patients (about one in ten) had seizures of various kinds—often changing in the same patient. With one exception these 8 patients exhibited EEG abnormalities, including the most severe forms of dysrhythmia encountered in the series. The literature on epilepsy as a symptom of multiple sclerosis is compared with the writers' findings.

The seizures are assessed partly on the basis of qualitative focal principles, partly as a more general reaction to the spread and severity of the acute process like the symptomatic psychoses. Intellectual defects were the predominant mental symptoms in about one third. Despite slight or no disease activity, the dementia is accompanied by dysrhythmia in the majority of cases. Affective symptoms were predominant in about half the cases. No significant relation was demonstrated between these symptoms and the EEG findings. Two patients developed psychosis during acute progression of the symptoms. Severe EEG changes accompanied the development of the psychoses.

Lastly, the writers summarize the psychopathology of the disease in the main features on the basis of the literature and discuss the pathogenesis. On the background of the incidence and nature of the mental symptoms and the pathoanatomical manifestation of the disease, the hypotheses suggesting a focal pathogenesis are considered more fruitful than the psychodynamic principles. 29 references. 1 table.

DISEASES AND INJURIES OF THE SPINAL CORD AND PERIPHERAL NERVES

96. *Familial Primary Amyloidosis With Nervous System Involvement.* ARTEN D. KANTARJIAN AND RUSSEL N. DEJONG, Ann Arbor, Michigan. Neurology, *3*: 399–409, June 1953.

The presence of nervous system involvement in amyloidosis has been recognized on only a few occasions.

A family is reported in which three members showed a similar syndrome consisting of the following clinical manifestations: (1.) Insidious onset of symptoms of relentlessly progressive, widespread disease after the second decade. (2.) Neurologic symptoms and signs compatible with a severe, progressive peripheral neuropathy. There was not only involvement of the motor nerves to the skeletal musculature and the sensory nerves, but also of the autonomic nervous system, resulting in sphincteric disturbances and trophic lesions. Accompanying this peripheral neuritis were spinal fluid changes characterized by a marked elevation in the total protein and nonspecific changes in the colloidal gold curve. (3.) Gastrointestinal symptoms characterized by anorexia, severe nausea, vomiting, constipation, abdominal pain, and loss of weight. (4.) Ocular changes consisting of loss of vision, vitreous opac-

ities, retinal exudates, progressive exophthalmos, and pupils which did not react to light. (5.) Endocrine changes manifested by enlargement of the thyroid with exophthalmos but a low basal metabolic rate together with amenorrhea and changes in the estrogen and 17-ketosteroid excretion in the women, and probably impotence in the man. (6.) A systolic murmur similar to that found in congenital heart disease. Postmortem examinations have been carried out on 2 of the 3 patients, but unfortunately, neither of the autopsies was complete and in neither was there adequate examination of the peripheral nerves. In both cases, however, there was evidence of diffuse primary amyloidosis.

The genetic nature of the disorder in this family cannot be disputed, and though specific information is known regarding only two generations, the disease may be assumed to be inherited as a simple Mendelian dominant. 13 references. 6 figures. —*Author's abstract.*

ELECTROENCEPHALOGRAPHY

97. *Neurosurgical and Neurologic Application of Depth Electrography.* HENRY W. DODGE, JR., ALLAN A. BAILEY, REGINALD G. BICKFORD, MAGNUS C. PETERSEN, CARL W. SEM-JACOBSEN, AND ROSS H. MILLER, Rochester, Minn. Proc. Staff. Meet. Mayo Clin. 28:188-191, March 1953.

The neurosurgeon and neurologist have the responsibility for evaluating depth electrography. No one minimizes the importance of electroencephalographic tracings obtained from the scalp and cortex; however, depth electrography introduces another diagnostic procedure which may overcome some of the disadvantages of previous methods. If the insertion of the depth electrodes is carefully planned, cortical stimulation may be unnecessary at the time of operation.

Depth recording also has its limitations. Two procedures are necessary: (1) the placing of the electrodes, and (2) the subsequent surgical procedures. Some minimal trauma to the brain substance and the vessels is a possibility and cannot be overlooked.

One of the first patients to undergo this procedure was a 29 year old woman with a convulsive disorder associated with psychotic behavior. The convulsions were grand mal in type. Depth electrography revealed an epileptic focus in the left frontal area, deeper than the area suggested by scalp electrography. Since removal of the deep focus the patient has had no further seizures.

Depth electrography may bring to the front new information concerning the deeper structures of the brain and their relationship to nervous and mental disease. 3 references. —*Author's abstract.*

98. *Metrazol Activation of the Electroencephalogram in Psychiatric Patients.* ALBERT N. BROWNE-MAYERS AND LEONARD R. STRAUB, New York, N. Y. Bull. New York Acad. Med. 29:30-31, January 1953.

Two groups of psychiatric patients were studied with pentylenetetrazole (metrazol): the first, those who on admission to the Payne Whitney Clinic manifested

mildly to moderately abnormal changes in the brain waves in the absence of neurologic disease, previous electric shock, or insulin therapy; the second, those whose predominant complaints centered around disturbances, in perception of self or the environment or who had acute rage reactions. These patients were called "epileptoid." The authors found that both groups of patients were more sensitive to pentylenetetrazole, injected intravenously at a rate of 20 mg. every 30 seconds for a total of 400 mg., than psychiatric patients who showed neither of the above abnormalities. Of the 26 control patients, 24 showed no further electroencephalographic changes when given pentylenetetrazole and 2 showed moderately abnormal responses to the drug. Of the 13 patients tested because of electroencephalographic disturbances, 2 showed no further changes with pentylenetetrazole, 5 showed moderately abnormal responses, and 6 showed epileptiform wave patterns. Twelve patients were tested because of "epileptoid" psychopathologic features, and 4 of these exhibited no further change with pentylenetetrazole, while 2 showed moderately abnormal responses and 6 epileptiform discharge. There was no epileptiform discharge in the control group. Of those with electroencephalographic abnormalities, 6 showed epileptiform wave patterns, and 2 of these had a grand mal seizure. Of the 6 patients in the "epileptoid" group who had epileptiform discharge with pentylenetetrazole, 1 had a grand mal seizure.

The authors believe that pentylenetetrazole is a sensitive tool for the evaluation of abnormalities in the brain waves of psychiatric patients. Although other workers have attributed electroencephalographic abnormalities to one or another psychiatric entity, the authors show that abnormalities were found in patients in any psychiatric diagnostic categories. Pentylenetetrazole proved useful in substantiating the diagnosis of epilepsy in one patient. This work points to the need for a broader understanding of electroencephalographic abnormalities in psychiatric patients.—*Author's abstract.*

99. *Electroencephalographic Studies of Infants and Children Who Acquired Intracranial Injuries at Birth.* ODD MÖRSTAD AND BIRGER R. KAADA, Norway. Neurology 3:544–549, July 1953.

The types and localization of EEG abnormalities were studied in children and young adults who had shown definite signs of brain hemorrhage or serious asphyxia at the time of birth.

About two thirds of the cases with an abnormal EEG showed *focal* cerebral disturbances, and in about three fourths of the same children the abnormalities consisted of discharges indicative of an *epileptogenic* lesion. The incidence of epileptiform discharges was about as high in children with intellectual defects and abnormal emotional behavior as in children suffering from epileptiform motor seizures. In either of these two groups of children, the left parieto-occipital region was the one most frequently affected. The possible explanation of this site of predilection of the cerebral injury at birth is discussed. 16 references. 2 figures. 1 table.—*Author's abstract.*

HEAD INJURIES

100. *Incidence of Epilepsy Following Craniocerebral Injury: Three-Year Follow-up Study.* C. WESLEY WATSON, Boston, Mass. A. M. A. Arch. Neurol. & Psychiat. *69*:831–34, December 1952.

In a follow-up study of 500 men who had had a craniocerebral injury during active combat service, satisfactory replies were received from 286 men three years after the injury; all these men had had a "penetrating head injury." Three years after the injury 119, or 41.6 per cent, had had epileptic seizures; in most cases the epileptic seizures developed within the first two years after injury, but in 18 cases the seizures developed in the third year after injury. Satisfactory data on the persistence of seizures were obtained from 53 of these 119 patients. Only 9 of these patients had been free from epileptic seizures for one year or more. In the other 44 patients seizures continued to occur in spite of the fact that with few exceptions, these patients were being treated with antiepileptic drugs—diphenylhydantoin (Dilantin®) and/or phenobarbital; 20 reported improvement, i.e., reduction in number or severity of seizures; 9 reported no change, and 15 that the seizures had become more severe or more frequent. A study of the family history of the patients with epileptic seizures showed no evidence of hereditary disposition to the disease. The findings in these cases and other reports in the literature indicate that the average person shows a definite liability to epilepsy resulting from cerebral trauma. 2 tables. 12 references.

101. *Intellectual Functions in Aphasic and Non-Aphasic Brain Injured Subjects.* RALPH M. REITAN. Neurology *3*:202–212, March 1953.

Since Hughlings Jackson's early consideration of the rôle of intelligence in aphasia, a considerable number of opinions and conclusions have appeared in the literature. The majority of investigators have agreed in essence with Jackson, believing that aphasia is a specific loss in speech and related symbolic functions rather than being a symptom, at least in part, of impaired general intelligence due to brain damage. Both Pierre Marie and Kurt Goldstein have presented the opinion, however, that aphasia represents a loss in general intelligence different in kind or degree from intellectual impairment from brain damage without aphasia. These previous conclusions have been based mainly on gross impressionistic observations of clinical material.

In the present experiment, intellectual functions of three groups of 18 subjects were assessed with the Rorschach Test. The groups consisted of brain-injured subjects with residual aphasia, brain-injured subjects with no aphasia, and hospitalized controls. The subjects were individually equated for age, education, and vocabulary. The aphasic and nonaphasic brain-injured subjects were equated for the severity of brain damage. Comparison of the two brain-injured groups with the controls gave statistically significant evidence of some intellectual impairment, probably related to a loss in abstraction. In comparing the aphasic and nonaphasic brain-injured subjects, no substantial differences were found. This absence of dif-

ferences was interpreted as indicating that the language disturbances in aphasia are not an integral aspect of the intellectual impairment due to brain damage. 17 references. 3 tables.—*Author's abstract.*

INTRACRANIAL TUMORS

102. *Misconceptions Leading to Delay in the Diagnosis of Intracranial Space-Taking Lesions.* WILLIAM R. CHAMBERS. Postgrad. Med. *13*:405–409, May 1953.

Cases have been presented which illustrate the mishaps and misconceptions in diagnosis of intracranial tumors found in a new practice of neurosurgery. The cases fall into four categories: (1) too great an emphasis on the psychiatric possibilities; (2) too little awareness of the possibility that a neurosurgical condition may exist; (3) a skepticism on the part of the patient or the doctor acting as an impediment to a sincere effort at diagnosis, and (4) failure to use or apply correctly easily used and readily available instruments of investigation.

For Reference Only

103. *Intracranial Sarcomas.* ERNA CHRISTENSEN, Copenhagen, Denmark and D. E. LARA, Buenos Aires, Argentina. J. Neuropath. & Exper. Neurol. *12*: 41–56, January 1953. Reports 25 cases. 7 figures. 1 table. 12 references.

NEUROPATHOLOGY

104. *Neuropathologic Lesions Following Lobotomy.* NAOMI RASKIN, GEORGE STRASSMAN, AND CHARLOTTE C. VAN WINKLE, Boston, Mass. Am. J. Psychiat. *109*: 808–816, May 1953.

The authors were interested in the study of the process of the repair of the wounds of the bilateral lobotomy and the factors that may have adversely affected it. They had found that the larger number of the patients died of causes not immediately related to lobotomy but that these conditions exerted an irritative effect on the wounds and retarded their healing. The authors believe the antibiotics should be used routinely. They found thickened infiltrated meninges, subdural and intracerebral hemorrhages, large cystic cavities with phagocytic activity going on at the periphery even in old cases, dilation and deformity of the frontal horns of the lateral ventricles, atrophy of the parvo-cellular areas of the nucleus medialis dorsalis, degeneration of the nerve-fibres at the distance from the surgical lesions, and numerous tiny areas of demyelinization not unlike those found in multiple sclerosis. The authors call attention to postlobotomy epileptic seizures and advocate the prophylactic use of dilantin. In their opinion, lobotomy is influenced by the state of health and of cerebral circulation of the patient to such a degree that the patient should be considered a medical as well as a psychiatric problem. They emphasize the fact that because of the technical difficulties more tissue is destroyed than the rationale of this treatment warrants and that added destruction may account for many symptoms beclouding the release of tension and anxiety achieved by the sectioning of the thalamofrontal fibers. 13 references. 10 figures.—*Author's abstract.*

book reviews

Sexual Behavior in the Human Female. ALFRED C. KINSEY, W. B. POMEROY, C. E. MARTIN, AND P. H. GEBHARD, Philadelphia, W. B. Saunders Co., 1953, 842 pages. Price $8.00.

Doctor Kinsey's latest study has made its appearance with all the unostentatiousness of a skyrocket! Now that the whole country has been treated to inspired "summaries" and "reports" in the daily press and the weekly and monthly magazines, the medical and other professional journals have been allowed by the publishers to see what the book *really* says. To this reviewer, at least it seems unfortunate that a serious scientific work of properly restricted interest should be ballyhooed by a highly respectable medical publisher as if it were another "Gone with the Wind" or "From Here to Eternity." Such, however, are the facts.

In spite of the way the publicity has been handled, however, there is no question of the value of the long and painstaking work of Doctor Kinsey and his collaborators here reported. The title, to be sure, is misleading. The volume reports a vast amount of detail as to the overt sexual behavior of slightly less than 6000 white women, mostly of high school education or better, mostly between the ages of 20 and 50, largely Protestant (12.3 per cent Catholic, 28.7 per cent Jewish), and predominantly from the eastern and middle western parts of this country. The fact that this group is not representative of American women as a whole is, of course, clearly pointed out by Doctor Kinsey himself. Nevertheless, here are data on women who are carrying on their day-to-day activities with at least reasonable success, who are not overtly in conflict with the law or in difficulties with their neighbors—who are, in short, at least moderately "well adjusted." It is this very point that makes the book valuable to the psychiatrist or marriage counselor, for example; the data, within their limitations, may be taken as guide-lines for the professional man, who too often sees only the emotionally disturbed, and may therefore acquire a skewed idea of what is within "normal" limits.

One feature that stands out is the difference in attitudes and practices of women born since 1920 and those of the older group, the younger women seeming to have "more deliberate approaches to sexual problems" (p. 299). The reasons for this change in attitudes since World War I are discussed by Doctor Kinsey, and are, of course, matters of general impression. In the younger group petting and premarital coitus are found more frequently, for example, with marital frigidity being less frequently reported. Apparently, too, the younger group begin petting earlier, and more of them carry it to orgasm. Doctor Kinsey points out the universality of petting and the fact that it is not unknown among other mammals than humans.

It seems clear, as we have long suspected, that legal sanctions are substantially less effective in controlling sexual conduct than the mores of the group and, especially, religious teachings. Particularly among the devout Catholic and the Jewish groups religious sanctions appeared the most important single factor, with the decade of birth a close second.

A chapter is devoted to psychologic factors in sexual response, this being largely on the Pavlovian level. Very little consideration is given to the esthetic, romantic and "non-erotic" overtones of sexual behavior throughout the volume—a fact which the psychiatrist is bound to consider a defect. However, the book purports only to describe overt behavior. Doctor Kinsey points out, however, some interesting psychologic differences between the sexes in this sphere.

Doctor Kinsey (who is, of course, an outstanding biologist), takes violent exception to the concept of "vaginal orgasm." He considers that in view of the anatomic and physiologic factors in sexual response, particularly the lack of sensory end-organs in the vagina, this term is incomprehensible. He states (*p. 582*), "Freud . . . contended that psycho-sexual maturation involved a subordination of clitoral reactions and a development of sensitivity within the vagina itself, but there are no anatomic data to indicate that such a physical transformation is possible." He interprets orgasm as a total reaction, involving, among others, "changes in pulse rates, blood pressure, breathing rates, peripheral circulation of blood, glandular secretions, changes in sensory capacities, muscular activity, and still other physiologic events." (p. 594.) The chapters on orgasm deserve careful study.

Finally, in reference to individual variations, Doctor Kinsey says (p. 543) "The sexual history of each individual represents a unique combination of these variables. We have never found an individual who was a composite of all the averages on all of the aspects of sexual response and overt activity . . . This is the most important fact which we can report on the sexual histories of the females who have contributed to the present study." The extensive bibliography (about 100 references) and the many charts and tables add much to the value of the work.

The volume is a thoroughly honest and sincere detailed study of the overt sexual behavior of a selected group of American women who are functioning in their respective capacities in the community. The group is the largest so far studied, and so far the most thoroughly studied. The data presented are valuable, and those who are professionally concerned with problems of human behavior are indebted to Doctor Kinsey and his co-workers. *Winfred Overholser, M.D.*

Psychiatry and Medicine. LESLIE A. OSBORN. New York, McGraw Hill Book Co. 1952. 194 pages. Price $7.50.

The author, who came to psychiatric teaching by way of general practice, chooses well as a subtitle for his book, "An Introduction to Personalized Medicine." Doctor Osborn, former head of the Department of Psychiatry at the University of Buffalo and presently Professor of Psychiatry at the University of Wisconsin, has given us a text for undergraduate medical students along new lines.

Very little space is given to a description of the psychoses and neuroses as such. Rather, he emphasizes the "patient-as-a-person" or "holistic" approach, the importance of considering all the aspects of the patient's life-experiences, and the factors in his present situation, together with the patient's attitude toward them.

Part one deals with Theoretical Considerations—the nature of illness, development, and social living. Part two considers Practical Applications—types of re-

action to life's experiences, the clinical study, and therapy. A short chapter on Preventive Medicine and Psychiatry, with a summary of outlines for use in teaching, concludes the volume.

The style is highly readable, the general attitude of the author practical, the aim to present psychiatry as an integral part of general medicine. Every medical student should find the book most helpful; many practitioners of general medicine would profit as well.—*Winfred Overholser, M. D.*

Thinking. An Introduction to Its Experimental Psychology. GEORGE HUMPHREY, New York. John Wiley and Sons, 1951. 311 pages. Price $4.50.

This book, by the Director of the Institute of Experimental Psychology at Oxford, is intended to give a critical treatment of the experimental work that has been done in studying intellectual processes of human beings and to serve as an introduction to research in this field.

Professor Humphrey traces the association theory from Thomas Hobbes' principle of contiguity to its reformulation in terms of the conditioned reflex and points out that the criticisms of the modern objective form of the theory are strikingly parallel to those made of the earlier form.

Four chapters are devoted to the Wurzburg group and their successor, Selz. There has been a tendency in modern psychology to neglect the work of these men, though they were concerned with a set of general problems that are still very much alive. The summary given here should be useful to students because it provides a preview of work basic to modern experimental thinking, the original sources of which are quite difficult to obtain. A discussion of the Gestalt theory of thought follows with emphasis upon its still developing nature and the problems as yet left unanswered. The next two chapters deal with the relation of thought to motor reaction and to language. The last topic to be treated is generalization which is defined as "the ability to discern and act upon similarities hidden beneath divergence. It is, at bottom, the ability to learn from experience."

The material is well organized and there is an excellent reference list. The footnotes, inevitable in a historical study, are not excessive. Professor Humphrey gets immediately into the subject under discussion without the superficial survey from Thales to the present which usually constitutes the first chapter of all reviews of experimental work.

The book should prove of value to psychologists interested in the historical development of current psychologic theories as well as to those particularly concerned with the experimental psychology of thinking. Its value, however, is limited by the fact that there is no attempt even to call the reader's attention to research dealing with the effects of emotion on thought processes.—*Margaret Mercer, Ph.D.*

Recovery From Aphasia. JOSEPH M. WEPMAN, New York. The Ronald Press Co. Price $4.50.

The title of this book, although somewhat optimistic, indicates the extreme value

of proper treatment in rehabilitation of a group of patients who are otherwise often doomed to chronic invalidism. In the treatment of aphasia, an organismic approach can often lead to a completely satisfactory restoration of language function. Doctor Wepman envisages a multidisciplinary type of teamwork in this problem. The medical specialist in this field should have a good background in neurology, psychology, education, and speech pathology. Ideally the services of specialists in all these fields might be used in a coordinated program. In practical experience with aphasic veterans of World War II, the author found the best therapist was most often an educator or psychologist without previous training in this particular area. "His attributes should include the ability to overcome the lack of initiative of the aphasic adult; an alertness to behavior changes, frustration and impulsivity; the ability to obtain and maintain a good learning climate and to recognize the self-concept of the patient; and the ability to structure the learning toward acceptable patient-recognized goals." The author devotes ample discussion to the rôle of ancillary therapists such as the nurse, the occupational therapist, the physical therapist, and the members of the patient's family.

One of Dr. Wepman's most interesting observations is the absence of aphasia in left-handed patients with lesions of the right hemisphere. Of 696 patients with left hemiplegia, none had residual aphasia. Of 2 patients with right hemiparesis known to be left-handed prior to injury, both had aphasia. The author believes that language deficits following damage to the right hemisphere either are of the nature of dysarthria or, if aphasia-like, last only a short time and are overcome spontaneously.

This book should be of value to all who are concerned with the professional care of the aphasic, including neurologists, psychiatrists, psychologists, speech pathologists, and nurses. There are also several sections which should serve as a guide to the family in the home care of these patients.—*George D. Weickhardt, M. D.*

Conferences on Drug Addiction Among Adolescents. New York, The Blakiston Company, 1953. 320 pages. Price $4.00.

This volume records two of the many fruitful multidisciplinary conferences on varied topics sponsored by The Josiah Macy, Jr., Foundation.

These particular conferences had to do with a topic which one hears so much of nowadays—drug addiction among adolescents. Over 50 persons participated, each one interested in some phase of the problem and competent to speak on his field; there were pharmacologists, psychiatrists, school principals, judges, police, and sociologists, to mention only a few.

It is obviously difficult to summarize a volume of this type, which reports a pretty free give-and-take of discussion. A few points, however, may be touched upon. The problem appears to be "primarily a sociological, psychological and economic problem, and secondarily a medical one" (p. 108). That it is a widespread one seems agreed, but no one has inclusive statistics. One police inspector reported about 600 arrests of adolescent addicts in New York City per year, but how representative or conclusive this figure is, no one can say definitely. For this

reason Dr. Haven Emerson suggested the eminent desirability of making drug addiction a reportable disease. Certainly, the state hospital figures give no idea of the problem: it was stated that from 1946 to 1951 only 55 patients were admitted to the New York state hospitals as a result of opium or its derivatives. Finally, it was urged that the peddler be "taken out of circulation," but that the addict be removed from the criminal category.

Much useful information is found between the covers of this book. It merits careful reading.—*Winfred Overholser, M. D.*

Books Received for Review

The Psychopathic Delinquent and Criminal. GEORGE N. THOMPSON, Springfield, Ill. Charles C Thomas, 1953. 157 pages. Price $4.50.

Children of Divorce. J. LOUISE DESPERT, New York. Doubleday & Co., 1953. 282 pages. Price $3.50.

The Conception of Disease. WALTHER RIESE, New York. Philosophical Library, 1953. 120 pages. Price $3.75.

Cybernetics: Transactions of the Ninth Conference, 1952. New York. Josiah Macy, Jr., Foundation, 1953. 184 pages. Price $4.00.

The Moral Theory of Behavior. FRANK R. BARTA, Springfield, Ill. Charles C Thomas, 1952. 35 pages.

Fundamental Psychiatry. JOHN R. CAVANAGH AND JAMES B. MCGOLDRICK, Milwaukee, Wis. Bruce Publishing Co., 1953. 582 pages. Price $5.50.

NOTES AND ANNOUNCEMENTS

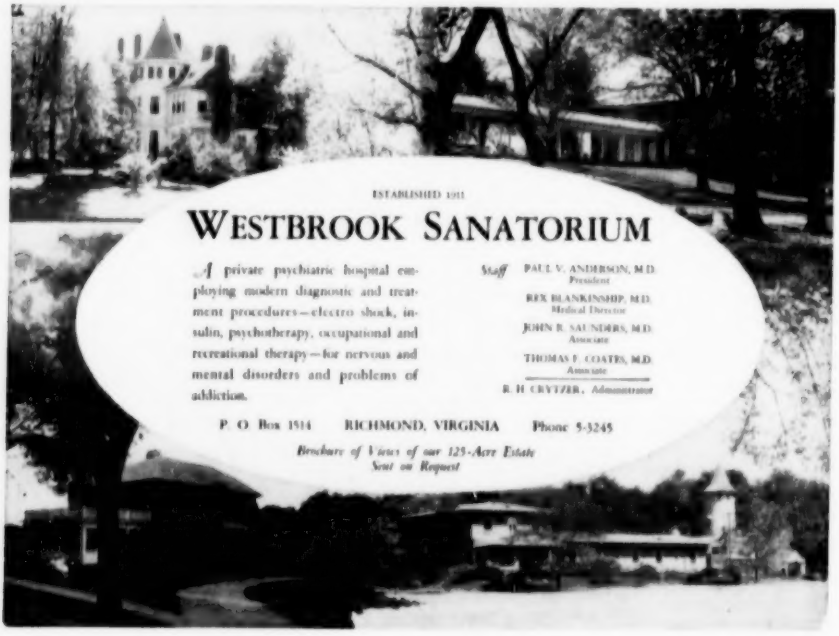
The QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY will be combined with the JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY beginning with the January, 1954, issue. This combined edition of the two publications will include advanced clinical and experimental reports, papers concerning all phases of psychiatric service and research—biologic, chemical, psychologic, physiologic, and social, and abstracts of the more significant articles in the periodical medical literature of the Americas and Europe.

Doctor Winfred Overholser will continue as editor of the QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY, and Doctor Arthur Sackler and Doctor Félix Martí Ibáñez will go on as national and international editors, respectively, of the JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY. Also, the same editorial boards will remain for each of the journals.

The QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY is glad to welcome to the field of psychiatric journalism a new periodical devoted to psychotherapy—ACTA PSYCHOTHERAPEUTICA, PSYCHOSOMATICA ET ORTHOPAEDAGOGICA.

Under the general editorship of E. A. D. E. Carp and B. Stokvis, both of Leyden, a distinguished international board of editors and collaborators will serve. Among the former we find F. Alexander and F. Dunbar, and among the latter Brenman, T. French and E. Weiss of the United States, as well as such well-known names from other countries as Bustamente, H. Ey, Krapf, Kretschmer, Seguin and Wittkower. The journal is published by S. Karger, Basel and New York (c/o Stechert-Hafner, Inc., New York City).

The QUARTERLY REVIEW extends to the editors and staff of the new journal all good wishes for success.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